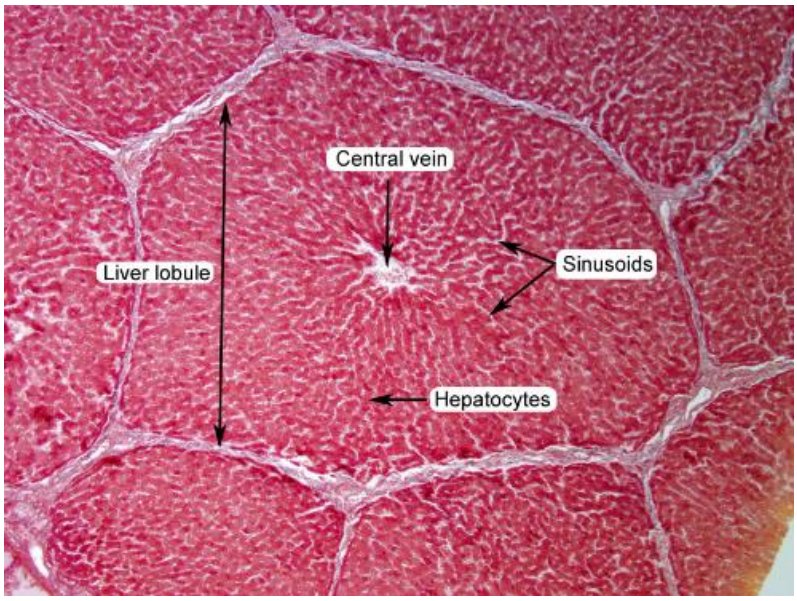
MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
STATE UNIVERCITY
«UZHHOROD NATIONAL UNIVERCITY»
MEDICAL FACULTY 2

DEPARTMENT OF FUNDAMENTAL MEDICAL DISCIPLINES

Histological Workbook

(part two)

"SPECIAL HISTOLOGY AND EMBRYOLOGY"



Student

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Uzhhorod 2019

Methodological developments have been recommended to the edition at the meeting of "Department of Basic Medical Disciplines„ (protocol №1 from 29.08.2017)

Histological Workbook. Part II. Methodological developments for laboratory classes/ Dobryanska E.S., Petrychko O.I. – Uzhhorod, 2017. – 255p.

Reviewers: professor Koval H.M., assistance professor Rostoka L.M.

This text contains the concise thorough presentation of Cytology, Embryology, General and Special Histology, based on modem information of functional morphology of cells, tissues, different organs and systems. This text was created on the basis of the systematized lecture course on Histology, Cytology and Embryology which is delivered at the Histology, Cytology and Embryology Department of State institution for the students of the Faculties of Medicine. Edition is oriented to the effective learning or revision of course of Cytology, Embryology, General and Special Histology and meant for the students in the health professions and advanced undergraduates.

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MODULE 2
"SPECIAL HISTOLOGY AND EMBRYOLOGY"

Module 2. Special histology and embryology.
Modular Content

Submodule 5
1. Special histology and embryology of nervous system.
2.Special histology and embryology of sensory systems.
3.Special histology and embryology of skin and its derivates.

Submodule 6
1. Special histology and embryology of cardiovascular system.
2. Special histology and embryology of haemopoetic organs.

Modul 3. **Special histology and embryology of the internal organs.**
Modular Content

Submodule 7
1.Special histology and embryology digestive system.

Submodule 8
1. Special histology and embryology respiratory system.
2. Special histology and embryology urinary system.
3. Special histology and embryology male reproductive system.
4. Special histology and embryology female reproductive system.
5. Special histology and embryology endocrine system.

Credit and modular educational system encourages students to study systematically during the school year.
The types of classes according to the curriculum are:
A) lectures;
B) practical training;
B) independent student's work.
Topics lectures reveal issues relevant sections of histology, cytology and embryology.
Practical exercises include:
1.Reseaching students histological structure of tissues and organs in the study of histological preparations.
2. Situational tasks, with clinical and histological orientation.
In practical lessons students painting and describe the structure of the histological preparations in albums, making it as a practice protocol.Adopting the theme is controlled at the workshops to meet specific objectives, learning content modules - lessons on practical outcomes. Used such tools for diagnosing the level of students: oral interviews, blank tests, solving situational problems for determining the level of assimilation of knowledge, analysis and evaluation of research results of histological preparations and electron micrograph for control of practical skills.Final control module or block is on their end. Assessment of students with discipline and a rating assigned by bahatobalnoyu scale as an average score of relevant learning modules and a determination by the ECTS system and the scale adopted in Ukraine.

MODULE 2 «SPECIAL HISTOLOGY AND EMBRYOLOGY»

Modular Content

Submodule 5
1. Special histology and embryology of nervous system.
2.Special histology and embryology of sensory systems.
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Submodule 6
1. Special histology and embryology of cardiovascular system.
2. Special histology and embryology of haemopoetic organs.

Criteria for evaluation of knowledge and skills students

Module 2 «SPECIAL HISTOLOGY AND EMBRYOLOGY»		
1	**2**	**3**
Practical lessons **(№№ 24 -37)**	**Mark** **Points**	**Criteria**
	5marks	The theoretical content of the topic lessons learned perfectly, all the necessary practical skills with lessons mastered the material, provided all program

	7points	objectives in the album performed better, the quality of their estimated maximum possible score.
	4 marks **5 points**	The theoretical content of the topic lessons learned in full with no gaps, all the necessary practical skills with lessons mastered the material, provided all program objectives in the album done, the quality of their performance rated a score close to maximum.
	3 marks **3 points**	The theoretical content of the topic classes mostly learned, without significant gaps, some practical skills learned enough material formed, provided all program objectives in the album done, the quality of any of them have not been evaluated maximum score, some tasks performed correctly.
	2 marks **0 points**	The theoretical content of the topic lessons learned in part, the gaps have significant character, the necessary practical skills learned material is mainly formed by the majority provided by the tasks performed on the album, some of the assignments contain errors. The theoretical content of the topic lessons learned in part, the gaps are substantial in nature, some practical skills are not formed, many provided by the tasks in the album are not met, or the quality of their performance rated a score close to the minimum. The theoretical content of the topic lessons not learned the necessary practical skills are not formed, most of the tasks under the program in the album is not performed or the quality of their performance rated a score close to the minimum, all tasks performed on the album contain gross errors, or generally not enforced (no album).
Concluding lessons of the submodule 5 and 6 **(№№ 5, 10,16,21)**	**5marks** **14points**	Answer theoretical questions impeccable (2 points) test tasks performed at 100% (20 tests of 0.3 points = 6 points), diagnosis of histological preparations and electron microphotograph performed flawlessly, the quality of reports describing their estimated maximal score (score 1).
	4 marks **9points**	Answer theoretical questions are very accurate (1.6 points), test tasks performed on 80-90% (16-19 tests on 0.3 points = 4.8-5.7 points), diagnosis of histological preparations and electron microphotograph done correctly, the quality of reports describing their estimated score, close to the maximum (by 0.8 points).
	3 marks **7 points**	Answer theoretical questions basically accurate (1.2 points), test tasks performed on 70-80% (14-16 tests on 0.3 points = 4.2-4.8 points), diagnosis of histological preparations and electron microphotograph done with some errors (by 0.6 points) the quality of any description of the protocols have not been evaluated in very well and above. Answer theoretical questions are not accurate (0.8 points), test tasks performed on 60-70% (12-14 tests on 0.3 points = 3.6-4.2 points), diagnosis of histological preparations and electron microphotograph carried out with errors (by 0.4), the quality of any describing the protocols have not been evaluated in well and above. Answer theoretical questions with errors (0.2 points), test tasks performed on 50% (10 tests on 0.3 points=3.0points), diagnosis of histological preparations and electron microphotograph carried out with considerable errors (by 0.2 points) or inaccurate, the quality of any of the protocols descriptions have not been evaluated on a satisfactory or higher.

	<u>2marks</u> **0points**	The answer to your question is not theoretical, test tasks performed at least 50% (8 and less tests, up to 2 points), diagnosis of histological preparations and electron microphotograph performed inaccurately, with gross errors, the quality of any description of the protocols have not been evaluated in sufficient and higher. Theoretical knowledge is missing, test tasks performed at least 40% (6 and less tests), diagnosis of histological preparations and electron microphotograph not done, no reports describe them.
Final module control (practical part)	**40 points**	Answers to tests of unmistakable and assessed the maximum possible score (40 x 0.5 points = 20 points), two reports describe the histological preparations and 2 electronic microphotograph meet the standard and the estimated maximum possible score (4 x 5 points = 20 points).
	37-39	Answer to the questions most accurate tests and evaluated close to the maximum score (18-19,5 points), two reports describe the histological preparations and 2 electronic microphotograph close to the standard and total assessed close to the maximum score (4) or / and above (5 points).
	33-36	Answers to the most accurate tests and assessed a high score (16-18 points), two reports describe the histological preparations and 2 electronic microphotograph with irrelevant comments and appreciated mediocre score (3) or / and above (4.5).
	29-32	Answers to the test task is not always accurate and assessed mediocre score (14-16 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracies and evaluated a low score (2) and / or higher (3,4,5).
	25-28	Answers to tests of inaccurate and evaluated a low score (12-14 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracies and evaluated a low score (1) or / and above (2,3,4,5).
	11-24	Answers to the test tasks in the most false and evaluated below the passing score (6-12 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracy (or error) and estimated scores from 0 to 2.
	0-10	Answers to the test tasks in the most erroneous, assessed the lowest score (less than 6) or absent, two reports describing the histological preparations and 2 electronic microphotograph false, assessed the lowest scores (0-1) or absent, or the student refused to perform the task.
Final module control (Theoretical part)	**40**	Theoretical Answers (6) on test questions perfect, estimated the maximum possible score (3 x 8 points = 24 points and 3 x 5.3 =16 points), all necessary program sections mastered better, with answers widely used abstract lectures and supplementary material.
	37-39	The theoretical answer to the question best, contain small errors, evaluated close to maximum points (7-8 and above), provided all program sections discipline mastered very well, with answers applying abstract lectures and supplementary material.
	33-36	The theoretical answer to the questions are good, with some inaccuracies, mostly assessed by high scores (6-7 and above), provided all program sections discipline mastered equally well, with answers applying abstract lectures.
	29-32	The theoretical answer to the question of errors, evaluated mainly mediocre scores (5-4 and above), provided the individual program sections discipline mastered uneven, with answers trying to apply abstract lectures.
	25-28	The theoretical answer to the question of substantial errors, mainly low valued points (3-4 and above), provided all program sections discipline

		mastered unevenly, with the answer does not apply additional material.
	16-24	The theoretical answer to the question of gross errors, evaluated mainly low scores (2-3 and above), provided the individual program sections discipline is mastered, the student is not focused on basic concepts or refuses to comply.
	0-15	The theoretical answer to the question incorrect, missing or student refuses to comply, the lowest estimated scores (0-4) provided the program sections discipline is mastered, the student does not have abstracts of lectures.

Before drawing final control module with an admitted students who have fulfilled all the missed lectures, practical classes, protocols drawn up independent work and took at **least 53 points** for the assessment of current performance.

Together it must be no less 53 points. The maximum number of points that a student can earn for practical classes is 120 points. The total number of points for the module is 200points or less (practical classes (min 54.5 – max 120points) + histopreparates (min 3- max 5 points) + electronograms (min 3- max 5 points) + MCQ control (min 15 – max 20 points).

Scale of assessments for students

Scores ECTS	statistic
A	Top 10% students
B	Next 25% of students
C	Next 30% of students
D	Next 25% of students
E	The last 25% of students
Fx	Re-exam
F	Mandatory re-training

Grading scale in Ukraine and its compliance with ECTS:

5 (excellent) – A (180-200points)
4 (good) - B (164- 179points)
4(good) - C (139 – 163 points)
3 (satisfactory) – D (128- 138points)
3(satisfactory) - E (120-127 points)
2 (Poor) - FX (70- 119points)
2 (Poor) – F (0-69 points)

THEMATIC PLAN OF LECTURES

№	Theme	hours
1.	Sense organs. Cardiovascular system.	2
2.	Skin and its derivates	2
3.	Cardiovascular system.	2
4.	Organs of haemopoesis and immune system.	2
In all		8

THEMATIC PLAN OF PRACTICAL TRAINING

№	Theme	hours

24.	Spinal ganglion. Nerve. Spinal cord.Autonomic nervous system.	2
25.	Central nervous system. Cortex of brain. Cortex of cerebellum.	2
26.	Sense organs. The Eye. Development. Tunics.	2
27.	Sense organs. Neural tunic of the eye (retina).	2
28.	Histology of ear.	2
29.	Skin and its derivates.	2
30.	**The control of mastering of the semantic module 2. "Special histology and embryology neural systems, sense organs, skin and its derivates."**	2
31.	Circulatory system. Arteries. Microcirculatory bed.	2
32.	Circulatory system. Lymphatic vessels and veins**.**	2
33.	Structure of the heart.	2
34.	Organs of haemopoiesis and immune system: bone marrow, thymus.	2
35.	Secondary organs of haemopoiesis. Spleen. Lymph and hemolymph nodes.	2
36.	Immune response. Macrophages.	2
37.	Haemopoiesis.	2
38.	**The control of mastering of the semantic module 2. "Special histology and embryology of the circulatory system and organs of haemopoiesis and immune system"**	2
39-40	**THE FINAL CONTROL OF MASTERING OF THE MODULE 2 «SPECIAL HISTOLOGY AND EMBRYOLOGY» Theoretical part.**	4
In all		34

Tasks for students' independent work.

№	Theme	hours
1.	Development of circulatory system.	3
2.	Embryonic haemopoiesis.	2
3.	Development of nervous system.	2
	In all	7

The distribution of points on the topics and types of control.

	Scores(max)	
	One lessons	**In all**
Module 2.		
Practical lessons №№ 24-37	7	112
The control of mastering of the semantic module № 30	6	6

The control of mastering of the semantic module № 38	6	6
Students' independent work.		6
THE FINAL CONTROL OF MASTERING OF THE MODULE 2	80	80
In all		200

MODULE 2. TEST ON TOPIC "SPESIAL HISTOLOGY"

1. Nerve system: general morphofunctional characteristic, classification (structural and functional).
2. Simple and complex somatic reflex arc, principal compounds.
3. Morphological and functional peculiarities of spinal node: sensory neurons and neuroglial compounds.
4. Autonomic (vegetative) nerve system: structural peculiarities. Vegetative ganglia: cellular structure and disposition. Reflex arc: special features.
5. Blood-brain barrier.
6. Cerebral cortex. Morphofunctional characteristic, cyto- and myeloarchitectony. Gliocytes of the cortex.
7. Cerebellum: general structure and functions. Cerebellar cortex, neurons. Interneuronal communications. Gliocytes of the cerebellum.
8. Spinal cord: general morphofunctional characteristic. Grey matter (nuclei and their cells compounds). Gliocytes.
9. Peripheral nerve system. Regeneration of nerve after the damage.
10. Morphological and functional peculiarities of spinal node: sensory neurons and neuroglial compounds.
11. Autonomic (vegetative) nerve system: structural peculiarities. Vegetative ganglia: cellular structure and disposition.
12. Autonomic (vegetative) reflex arc: special features.
13. Analyzers and their principle portions. Sense organs (classification due to the origin and structure of the receptor cells).
14. Visual organ. Eyeball: general structure, tunics.
15. Fibrous and vascular tunics of eyeball, their portions, structure and functions.
16. Cornea: microscopic and histochemical characteristic.
17. Inner eye tunic. Retina: nerve cells compounds. Retinal detachment.
18. Ultrastructural and cytochemical characteristic of the photoreceptive cells.
19. Lens.Structure and function.
20. Ciliary body. Structure and function.
21. Iris. Structure and function.
22. Eye: dioptric and accomodative apparatus.
23. Development of the eye.
24. Retina. Structure and function. Retinal detachment.
25. Audiovestibular organ. Cochlear membranous labyrinth (structure and functions). Corti's organ: histophysiology. Which cells registered high and low frequency sound (voice)?
26. Vestibular organ. Vestibular portion of the membranous labyrinth: disposition, structure and functions of the utricle and saccule macules and ampullary crests. Structure and function.
27. Structure and functions of the skin.
28. Structure and functions of epidermis. Physiologic regeneration of epidermis.
29. Dermis. Structure and function.
30. Hypodermis. Structure and function.
31. **Hairs**. Structure and function.
32. **Nails**. Structure and function.
33. Sweat glands. Structure and function.
34. Sebaceous glands. Structure and function.
35. Vessels classification. Structure and functions of the arteries.
36. Elastic arteries. Structure and function.
37. Elastic carcass (stroma) of aorta. Structure and function.
38. Elastic-muscular arteries. Structure and function.
39. Muscular arteries. Structure and function.
40. Classification, structure and functions of the capillaries.
41. Three types of blood capillaries.
42. Arterioles. Structure and function.
43. Venules. Structure and function.

44. General structure of capillaries.
45. Anastomosis. Structure and function.
46. Unmuscular (atypical) veins. Structure and function.
47. Strucutre, classification and functions of the veins.
48. Muscular veins with weak development of muscular elements.
49. Muscular veins with strong development of muscular elements.
50. Lymphatic vascular system (lymphatic capillaries, lymphatic collecting vessels, lymphatic duct).
51. Lymphatic capillaries. Structure and function.
52. Lymphatic collecting vessels. Structure and function.
53. Lymphatic duct. Structure and function.
54. Heart tunices: their structure and functions.
55. Heart. Conductive system (structure and function pacemaker (nodal) cells and Purkinje fibers).
56. Endocardium. Structure and function. Particular qualitis of blood supply (perfusion) in endocardium.
57. Heart. Contractile cardiac cells.
58. Thymus: structure and functions.
59. Structure and function the cortex of thymus.
60. Structure and function the medulla of thymus.
61. Blood-thymus barrier.
62. Involution of the thymus (age involution, acute (stress) involution, status thymico-lymphaticus).
63. Red bone marrow: structure and function.
64. Megakaryocytes (structure and function).
65. Erythroblastic islets.
66. Antigen-independent and antigen-dependent proliferation and differentiation T- and B- lymphocytes.
67. Lymph nodes: structure and function.
68. Secondary lymphatic nodule: structure and function.
69. The sinuses of the lymph nodes. Structure and function.
70. Outer cortex and deep cortex of lymph nodes. Structure and function.
71. Medulla of lymph nodes. Structure and function.
72. Spleen: structure and function.
73. White pulp of spleen: structure and function.
74. Red pulp of spleen: structure and function.
75. The sinuses of the spleen. Structure and function
76. Spleen blood supply (open and close system of blood circulation).
77. Antigen-dependent proliferation and differentiation of T- and B-lymphocytes, which ensure the immunological responses.
78. Microenvironment of T- and B- zones in the secondary organs of hemopoiesis and immune defense.
79. Cells co-operation in the body's immune response.
80. Characteristic of T lymphocytes (T cells).
81. Characteristic of B lymphocytes (B cells).
82. Characteristics of human immunoglobulins.
83. Characteristic of the plasma cells.
84. Immune responses to antigens.
85. Basic types of specific immune responses.
86. .Embryonic (prenatal) hemopoiesis.
87. Stem cells. The basic properties of stem cells.
88. Postnatal hemopoiesis.Physiological regeneration of blood.
89. Erythropoiesis. Process of development of erythrocytes. Regulation of erythropoiesis.
90. Granulopoiesis. Process of development of granulocytes . Regulation of granulopoiesis.
91. Theory of hemopoiesis.

THE LIST OF SPECIMENS

1. Brain cortex.
2. Cerebellum.
3. Spinal cord.
4. Spinal node.
5. Nerve (transverse section in human skin).
6. Intramural nerve plexus.
7. Cornea.
8. Wall of the eye.
9. Cochlear axial section.
10. Organ of Corti.
11. Muscular artery.
12. Elastic artery: aorta.

13. Muscular vein.
14. Arterioles, venules, capillaries.
15. Lymphatic vessel.
16. Heart: myocardium.
17. Heart: endocardium. Purkinje fibers.
18. Bone marrow smear.
19. Thymus.
20. Lymph node.
21. Spleen.

THE LIST OF ELECTRON MICROGRAPHS

1. Brain cortex nerve cells. Fig. 5
2. Cerebral cortex protoplasmic astrocyte. Fig. 7.
3. Brain cortex oligodendrocyte. Fig. 8.
4. Spinal cord grey matter. Fig. 3
5. Spinal canal ependyma. Fig. 4
6. Chief cell of the proper stomach gland. Fig. 44.
7. Parietal cell of the proper stomach gland. Fig. 45.
8. Accessory mucocyte. Fig. 46.
9. Columnar brushed cells. Fig. 49.
10. Columnar nonbrushed cells. Fig. 51.

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Module 3 « Special histology and embryology of the internal organs».

Modular Content

Submodule 7

1.Special histology and embryology digestive system.

Submodule 8

1. Special histology and embryology respiratory system.
2. Special histology and embryology urinary system.
3. Special histology and embryology male reproductive system.
4. Special histology and embryology female reproductive system.
5. Special histology and embryology endocrine system.

Criteria for evaluation of knowledge and skills students

Module 3 «Special histology and embryology of the internal organs».		
1	**2**	**3**
Practical lessons (№№ 41 -58)	**Mark Points**	**Criteria**
	5marks 7points	The theoretical content of the topic lessons learned perfectly, all the necessary practical skills with lessons mastered the material, provided all program objectives in the album performed better, the quality of their estimated maximum possible score.
	4 marks 5 points	The theoretical content of the topic lessons learned in full with no gaps, all the necessary practical skills with lessons mastered the material, provided all program objectives in the album done, the quality of their performance rated a score close to maximum.
	3 marks 3points	The theoretical content of the topic classes mostly learned, without significant gaps, some practical skills learned enough material formed, provided all program objectives in the album done, the quality of any of them have not been evaluated maximum score, some tasks performed correctly.

	<u>2 marks</u> **0 points**	The theoretical content of the topic lessons learned in part, the gaps have significant character, the necessary practical skills learned material is mainly formed by the majority provided by the tasks performed on the album, some of the assignments contain errors. The theoretical content of the topic lessons learned in part, the gaps are substantial in nature, some practical skills are not formed, many provided by the tasks in the album are not met, or the quality of their performance rated a score close to the minimum. The theoretical content of the topic lessons not learned the necessary practical skills are not formed, most of the tasks under the program in the album is not performed or the quality of their performance rated a score close to the minimum, all tasks performed on the album contain gross errors, or generally not enforced (no album).
Concluding lessons of the submodule 7and 8 **(№№ 49,58)**	**<u>5marks</u>** **12points**	Answer theoretical questions impeccable (2 points) test tasks performed at 100% (20 tests of 0.3 points = 6 points), diagnosis of histological preparations and electron microphotograph performed flawlessly, the quality of reports describing their estimated maximal score (score 1).
	<u>4 marks</u> **7 points**	Answer theoretical questions are very accurate (1.6 points), test tasks performed on 80-90% (16-19 tests on 0.3 points = 4.8-5.7 points), diagnosis of histological preparations and electron microphotograph done correctly, the quality of reports describing their estimated score, close to the maximum (by 0.8 points).
	<u>3 marks</u> **5points**	Answer theoretical questions basically accurate (1.2 points), test tasks performed on 70-80% (14-16 tests on 0.3 points = 4.2-4.8 points), diagnosis of histological preparations and electron microphotograph done with some errors (by 0.6 points) the quality of any description of the protocols have not been evaluated in very well and above. Answer theoretical questions are not accurate (0.8 points), test tasks performed on 60-70% (12-14 tests on 0.3 points = 3.6-4.2 points), diagnosis of histological preparations and electron microphotograph carried out with errors (by 0.4), the quality of any describing the protocols have not been evaluated in well and above. Answer theoretical questions with errors (0.2 points), test tasks performed on 50% (10 tests on 0.3 points = 3.0 points), diagnosis of histological preparations and electron microphotograph carried out with considerable errors (by 0.2 points) or inaccurate, the quality of any of the protocols descriptions have not been evaluated on a satisfactory or higher.
	<u>2marks</u> **0points**	The answer to your question is not theoretical, test tasks performed at least 50% (8 and less tests, up to 2 points), diagnosis of histological preparations and electron microphotograph performed inaccurately, with gross errors, the quality of any description of the protocols have not been evaluated in sufficient and higher. Theoretical knowledge is missing, test tasks performed at least 40% (6 and less tests), diagnosis of histological preparations and electron microphotograph not done, no reports describe them.
Final module control (practical part)	**40 points**	Answers to tests of unmistakable and assessed the maximum possible score (40 x 0.5 points = 20 points), two reports describe the histological preparations and 2 electronic microphotograph meet the standard and the estimated maximum possible score (4 x 5 points = 20 points).
	37-39	Answer to the questions most accurate tests and evaluated close to the maximum score (18-19,5 points), two reports describe the histological preparations and 2 electronic microphotograph close to the standard and total assessed close to the maximum score (4) or / and above (5 points).
	33-36	Answers to the most accurate tests and assessed a high score (16-18 points), two reports describe the histological preparations and 2 electronic microphotograph with irrelevant comments and appreciated mediocre score

		(3) or / and above (4.5).
	29-32	Answers to the test task is not always accurate and assessed mediocre score (14-16 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracies and evaluated a low score (2) and / or higher (3,4,5).
	25-28	Answers to tests of inaccurate and evaluated a low score (12-14 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracies and evaluated a low score (1) or / and above (2,3,4,5).
	11-24	Answers to the test tasks in the most false and evaluated below the passing score (6-12 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracy (or error) and estimated scores from 0 to 2.
	11-24	Answers to the test tasks in the most false and evaluated below the passing score (6-12 points), two reports describe the histological preparations and 2 electronic microphotograph with significant inaccuracy (or error) and estimated scores from 0 to 2.
	0-10	Answers to the test tasks in the most erroneous, assessed the lowest score (less than 6) or absent, two reports describing the histological preparations and 2 electronic microphotograph false, assessed the lowest scores (0-1) or absent, or the student refused to perform the task.
Final module control (Theoretical part)	**40**	Theoretical Answers (6) on test questions perfect, estimated the maximum possible score (6 x 6.6 = 40 points), all necessary program sections mastered better, with answers widely used abstract lectures and supplementary material.
	37-39	The theoretical answer to the question best, contain small errors, evaluated close to maximum points (5-6 and above), provided all program sections discipline mastered very well, with answers applying abstract lectures and supplementary material.
	33-36	The theoretical answer to the questions are good, with some inaccuracies, mostly assessed by high scores (4-5 and above), provided all program sections discipline mastered equally well, with answers applying abstract lectures.
	29-32	The theoretical answer to the question of errors, evaluated mainly mediocre scores (4-3-2 and above), provided the individual program sections discipline mastered uneven, with answers trying to apply abstract lectures.
	25-28	The theoretical answer to the question of substantial errors, mainly low valued points (3 and above), provided all program sections discipline mastered unevenly, with the answer does not apply additional material.
	16-24	The theoretical answer to the question of gross errors, evaluated mainly low scores (2 and above), provided the individual program sections discipline is mastered, the student is not focused on basic concepts or refuses to comply.
	0-15	The theoretical answer to the question incorrect, missing or student refuses to comply, the lowest estimated scores (0-4) provided the program sections discipline is mastered, the student does not have abstracts of lectures.

Before drawing final control module with an admitted students who have fulfilled all the missed lectures, practical classes, protocols drawn up independent work and took at **least 42 points** for the assessment of current performance. **The <u>maximum number</u> of points that a student can earn for practical classes is <u>120 points.</u> The total number of points for the module is 200points or less** (practical classes (min 54.5 – max 120points) + histopreparates (min 3- max 5 points) + electronograms (min 3- max 5 points) + MCQ control (min 15 – max 20 points).

Scale of assessments for students

Scores ECTS	statistic
A	Top 10% students
B	Next 25% of students
C	Next 30% of students
D	Next 25% of students
E	The last 25% of students
Fx	Re-exam
F	Mandatory re-training

Grading scale in Ukraine and its compliance with ECTS:

5 (excellent) – A (180-200points)
4 (good) - B (164- 179points)
4(good) - C (139 – 163 points)
3 (satisfactory) – D (128- 138points)
3(satisfactory) - E (120-127 points)
2 (Poor) - FX (70- 119points)
2 (Poor) – F (0-69 points)

The distribution of points on the topics and types of control.

	Scores(max)	
	One lessons	**In all**
Module 3.		
Semantic module 3		
Practical lessons №№ 37-58	3	39
The control of mastering of the semantic module № 36	6	6
Semantic module 4		
Practical lessons №№ 37-57	3	63
The control of mastering of the semantic module № 58	6	6
Students' independent work.		6
THE FINAL CONTROL OF MASTERING OF THE MODULE 3	80	80
In all		200

THEMATIC PLAN OF LECTURES

№	Theme	hours
1.	Oral cavity.	2
2.	Digestive system.	2
3.	Respiratory system.	2
4.	Urinary system.	2
5.	Reproductive system.	2

6.	Endocrine system.	2
	In all	12

THEMATIC PLAN OF PRACTICAL TRAINING

№	Theme	hours
41.	Digestive system. Development of mouth. Pharyngeal arches. Structure of lips, cheeks. Structure of gums, hard and soft palate. Tongue. Taste buds.	2
42.	Large salivary glands of cavity of mouth. Parotid salivary gland. Submandibular and sublingual glands. Tonsils.	2
43.	Embryoodontogenesis. Development of tooth. Micro- and submicroscopic structure of enamel, dentin, pulp chamber, cementum, parodont and periodont.	2
44.	Histology of esophagus and stomach.	2
45.	Histology of small intestine.	2
46.	Histology of large intestine. APUD-system.	2
47.	Structure and function of liver. Gall bladder.	2
48.	Structure and function of pancreas.	2
49.	**The control of mastering of the semantic submodule "Special histology and embryology of the digestive system"**	2
50.	Respiratory system. Nasal cavity. Olfactory region of the nasal cavity. Respiratory system. Lungs.	2
51.	Urinary organs. Nephron.	2
52.	Urinary organs. Urinary organs.	2
53.	Male reproductive system.	2
54.	Female reproductive system. Ovarium. Uterine tube.	2
55.	Female reproductive system. Uterus. Vagina. Menstrual cycle.	2
56.	Endocrine system. Hypothalamus. Pituitary gland (hypophysis). Pineal gland.	2
57.	Endocrine system. Adrenal gland. Thyroid and parathyroid glands.	2
58.	**The control of mastering of the semantic module 5. "Special histology and embryology of urinary, reproductive and endocrine system".**	2
59-60.	FINAL CONTROL of MASTERING of MODULE 3 "SPECIAL HISTOLOGY AND EMBRYOLOGY".	4
	In all	22

Tasks for students' independent work.

№	Theme	hours
1.	APUD-system.	3
2.	Development of digestive system.	5

3.	Large salivary glands of cavity of mouth.	5
4.	Preparing for the final control module 3.	10
	In all	23

MODULE 3. TEST ON TOPIC "SPESIAL HISTOLOGY"

1. Classification of the endocrine glands.
2. Hypothalamus nuclei, their endocrine functions, interconnections with hypophysis.
3. Magnocellular nuclei (supraoptic and paraventricular) of hypothalamus, structure, histophysiology, functions.
4. Neurosecretory cells of the parvocellular nuclei mediobasal hypothalamus, structure, histophysiology, functions.
5. Hypophysis: adeno- and neurohypophysis, hormones and their influence on the human body.
6. Neurohypophysis, hormones and their influence on the human body.
7. Adenohypophysis, hormones and their influence on the human body.
8. Development of the hypophysis.
9. Pineal gland: structure and functions.
10. Thyroid gland: structure and functions.
11. Secretory cycle of the follicular cells in thyroid gland.
12. Parathyroid glands: structure and functions.
13. Adrenal glands: structure and functions of the cortex and medulla.
14. Adrenal glands: structure and functions of the cortex.
15. Adrenal glands: structure and functions of the medulla.
16. Digestive tube: general structure, subdivision into portions due to the origin, structure and functions.
17. Lips, cheeks. Structure, histophysiology.
18. Hard and soft palate, gingiva. Structure, histophysiology.
19. Tongue. Taste buds. Structure, histophysiology.
20. Parotid glands, structure, histophysiology, functions.
21. Sublingual glands, structure, histophysiology, functions.
22. Submandibular glands, structure, histophysiology, functions.
23. Development of the tooth. Early stage.
24. Development of the tooth. Later stage.
25. Tooth enamel: microscopic and chemical compounds.
26. Tooth dentine: microscopic and chemical compounds.
27. Tooth cementum: microscopic and chemical compounds.
28. Structure and functions of tooth pulp and periodontum. Parodontium.
29. Pirogov's lymphoepithelial ring. Tonsilles: structure and functions.
30. Esophagus. General structure and microscopic peculiarities of the different portions of esophageal wall.
31. Stomach: walls, structure and tissues compounds.
32. Stomach glands: disposition, structure and cell compounds (exo- and endocrine cells types). Secretory cells (histophysiology).
33. Small intestine. Structure and functions. "Cript-villus" sytem: histophysiology and their participation in the parietal and intracavitary digestion.
34. Large intestine. Structure and functions.
35. Appendix: structure and function.
36. Rectum. Portions and their peculiarities.
37. Liver. Morphofunctional characteristic. Peculiarities of the blood supply.
38. Structure of classic hepatic lobule.
39. Intralobular hemocapillary (structure and functions).
40. Hepatic cords.
41. Hepatocytes (structure and functions).
42. The terms: "hepatic acinus" and "portal lobule".
43. Bile capillaries: structure and functions..
44. Gallbladder: structure and functions.
45. Pancreas. Structure and functions of the exocrine portion.
46. Pancreas. Structure and functions of the endocrine portion.
47. Pancreatic acinocytes: structural peculiarities. Structure of excretory ducts.
48. Cell types of the pancreatic islands, their morphofunctional characteristic.
49. Respiratory system: general morphofunctional characteristic.
50. Trachea: structure and functions.
51. Main (primary) bronchi, structure and functions.
52. Large bronchi, structure and functions.

53. Middl bronchi, structure and functions.
54. Small bronchi, structure and functions.
55. Terminal bronchioles, structure and functions.
56. The respiratory portion of the respiratory system (structural and functional units - acini).
57. Peculiarities of the bronchial wall due to the calibre. Characteristic features of the epithelium conducting system.
58. Structure and functions of the acinus – lung's morphofunctional unite.
59. Microscopic structure of the lung's alveolar wall.
60. Ultrastructure of aerohematic barrier. Conception about alveolar surfactant complex.
61. Structure and functions of the cortical nephron.
62. Endocrine apparatus of kidneys (the juxtaglomerular apparatus), structure and function.
63. Renal corpuscle, structure and function.
64. Filtration barrier of the renal corpuscle, structure and function.
65. Structure and function of the tubes of the nephron.
66. Ureter: structure and function.
67. Urethra: structure and function.
68.Urinary bladder: structure and function.
69. Development of the kidney.
70.Testis: structure and functions.
71. Prostate gland: structure and functions
72. Epididymis: structure and functions.
73. Convoluted seminiferous tubules: structure and functions.
75. The blood-testis barrier: structure and functions.
76. Endocrine function of the testis.
77. Spermatogenesis.
78. Ductus (vas) deferens: structure and functions.
79. Ejaculatory duct: structure and functions.
80. Development of the reproductive systems.
81. Ovary: structure and functions.
82. Ovarian follicles: structure and functions.
83. Mature (tertiary, preovulatory, Graafian) follicle: structure and functions.
84. Corpus luteum. Development of the corpus luteum. Types of the corpus luteum.
85. Ovarian follicular atresia.
86. Ovarian cycle.
87. Oogenesis.
88. Uterus: structure and functions.
89.Oviducts (uterine or Fallopian tubes) : structure and functions.
90.Menstrual (uterine) cycle.
91.Vagina : structure and functions.
92. Mammary gland: structure and functions. Lactation, nervous and endocrine regulation.

THE LIST OF SPECIMENS

1. Pituitary gland.
2. Pineal gland.
3. Thyroid gland.
4. Adrenal gland.
5. Human tongue. Filiform and fungiform papilla.
6. Human tongue. Foliate papilla.
7. Tooth development early stage.
8. Tooth development early stage. .
9. Parotid gland.
10. Submandibular gland.
11. Sublingual gland.
12. Esophagus.
13. Palatine tonsil.
14. Esophageo-gastric junction.
15. Fundus of the stomach.
16. Pyloric stomach.
17. Duodenum.
18. Small intestine (jejunum).
19. Large intestine.
20. Appendix. .
21. Human liver.

22. Pancreas.
23. Lungs.
24. Trachea.
25. Kidney.
26. Ureter.
27. Urinary bladder.
28. Testis.
29. Epididymis.
30. Prostate gland.
31. Ovarium of the cat.
32. Corpus luteum.
33. Uterine tube.
34. Uterus of the cat.

THE LIST OF ELECTRON MICROGRAPHS

1. Intestinal goblet cell. Fig.
2. Intestinal endocrine cell. Fig. 53.
3. Hepatocyte. Fig. 57.
4. Bile capillary. Fig. 60.
5. Exocrine pancreatocyte. Fig. 62, 63.
6. Insulocytes of pancreatic island. Fig. 64.
7. Apical portion of the ciliated epithelial cells. Epithelial layer of the nasal cavity respiratory mucosa. Fig. 65.
8. Alveolar sac alveoles. Respiratory portion of the lungs. Fig. 66.
9. Respiratory epithelial cell (alveolar cell of the I type). Fig. 67.
10. Large secretory epithelial cell - alveolar cell of the II type. Fig. 68
11. Aerohematic barrier. Fig. 69

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1.L. Carlos Junqueira, Jose Carneiro, Robert O. Kelley. Basic Histology. - 7th ed. Appleton and Lange. Norwalk, Connecticut, 1992, pp. 163-193, 467-496.

2.Inderbir Singh. Textbook of Human Histology with colour atlas. – 4th ed. Jaypee Brothers Medical Publishers (P) LTD, 2002, pp. 135-168.

3.Wheater P.R., Burkitt H.G., Daniels V.G. Functional Histology: a text and colour atlas. - 2nd ed. Longman Group UK Limited, 1987. - pp. 95-118, 316-342.

5. I. V. Bobrysheva, S. A. Kashchenko. Histology, Cytology, Embryology: Textbook.– Lugansk: Knowledge, 2011. – 528 p.

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The amount of points obtained by the student for the three modules is added and is divided into three**. This is the average amount of student points for a course in histology. This result is entered into the student's credit book in accordance with Grading scale in Ukraine and its compliance with ECTS:**

5 (excellent) – A (180-200points)
4 (good) – B (164- 179points)
4(good) – C (139 – 163 points)
3 (satisfactory) – D (128- 138points)
3(satisfactory) – E (120-127 points)
2 (Poor) – FX (70- 119points)
2 (Poor) – F (0-69 points)

NERVOUS SYSTEM

PERIPHERAL NERVE

The nervous system is the most complex in the human body and is formed by a network of more than 100 million nerve cells, assisted by the glial cells**.**

Functions of the nervous system:

1. integration (consolidation of parts of an organism in a single whole);
2.regulation and maintenance of homeostasis;

3. coordination of function of various organs and tissues;
4. interaction of an organism with our environment, both external and internal;
5.mental activity including thought, learning, and memory.

Subdivisions of the nervous system.

Anatomically nervous system is divided into:

1.***central nervous system*** (CNS) consisting of the brain and the spinal cord;

2***. peripheral nervous system*** (PNS) composed of nerve fibers, nerve ganglia, and nerve terminations.

Physiologically nervous system is divided into:

1***. somatic nervous system*** which controls mainly functions of an autokinesia;

2. ***autonomic nervous system*** which controls activity of the smooth muscles of the viscera, blood vessels, cardiac muscle of the heart, and secretory cells of the exocrine and endocrine glands, thus helping to maintain homeostasis.

The autonomic nervous system is subdivided into two functionally different divisions:

1. **The sympathetic nervous system** responds to impending danger, and is responsible for the increase of one's heartbeat and blood pressure, among other physiological changes, along with the sense of excitement one feels due to the increase of adrenaline in the system.

2. **The parasympathetic nervous system** is evident when a person is resting and feels relaxed, and is responsible for such things as the constriction of the pupil, the slowing of the heart, the dilation of the blood vessels, and the stimulation of the digestive and genitourinary systems.

Peripheral nerve In the peripheral nervous system the nerve fibers are grouped in bundles to form the nerves. The individual nerve fibers are held together by connective tissue organized into three components (fig.1):

1. **endoneurium** is a thin layer of loose connective tissue, surrounding each individual nerve fiber;
2. **perineurium** surrounds each bundle of nerve fibers;
3. **epineurium** includes the dense irregular connective tissue that surrounds a peripheral nerve. The nerves establish communication between brain and spinal cord centers and the sense organs and effectors (muscles, glands, etc.).

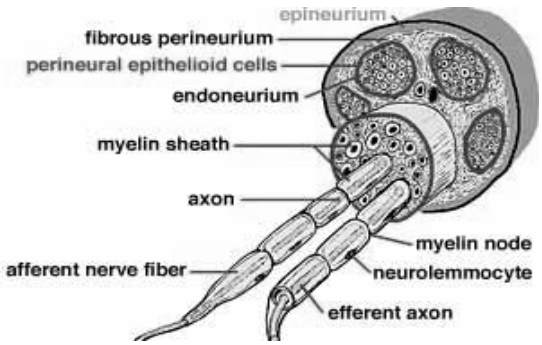


Figure 1. Schematic diagram of peripheral nerve.

Axonal Damage

Wallerian Degeneration. Wallerian degeneration refers to the changes that occur distally to the site of damage on an axon. Because protein synthesis occurs primarily in the neuronal cell body, the segment distal to the damaged site on the axon is affected profoundly. Initially, the axon swells up and becomes irregular. Later, the axon and the terminal are broken down into fragments that are phago-cytosed by adjacent macrophages and Schwann cells (Fig.2 A-D). Myelin is converted into fine drops of lipid material in the Schwann cells and is extruded from these cells; it is removed by macrophages in the PNS and microglial cells and invading macrophages in the CNS.

Alterations (similar to those mentioned earlier) may also be present in the proximal segment of the axon up to the first node of Ranvier.

Chromatolysis. Sectioning of an axon may produce changes in the cell body, and if the injury is close to the cell body, the neuron may degenerate. The cell body swells up due to edema and becomes round in appearance, and the Nissl substance gets distributed throughout the cytoplasm. This process is known as chromatolysis (Fig.2E). The nucleus moves from its central position to the periphery due to edema. The degenerative changes start within hours and are complete within a relatively short time (about a week).

Anterograde Transneuronal Degeneration. Anterograde transneu-ronal degeneration occurs in the CNS when damage to a neuron results in the degeneration of another postsynaptic neuron closely associated with the same function (Fig.2F). For example, damage to an optic nerve results in the degeneration of the lateral geniculate neurons receiving inputs from this nerve.

Retrograde Transneuronal Degeneration. Retrograde transneu' ronal degeneration occurs in neurons sending inputs to an injured neuron. In this situation, terminals of the neuron synapsing with a chromatolytic neuron withdraw and are replaced by processes of glial cells. The neuron, from which the inputs to the chromatolytic neuron arise, eventually degenerates (Fig.2 G).

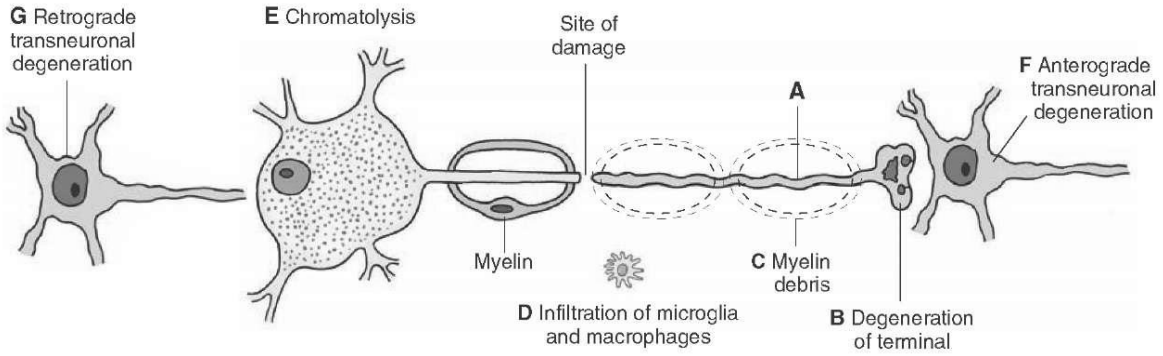


Figure 2. Schematic diagram of **regeneration** peripheral nerve.

Recovery of Neuronal Injury (Regeneration)

In the adult CNS**,** if the damage is not severe and some neuronal cell bodies are spared, sprouting of axons does occur, but this process ceases within a short time (about 2 weeks). Astrocytes proliferate at the site of injury in a random fashion and form a scar which acts as a barrier for axonal sprouts. Furthermore, astrocytes may not release growth factors that are needed for axonal growth, and oligodendrocytes

may release substances that retard axonal growth. In this situation, regeneration of axonal tracts does not occur, and normal functions of the neurons are not restored. However, in peripheral nerves, an axon can regenerate satisfactorily if the endoneurial sheaths are intact. In this situation, the regenerating axons reach the correct destination, and the chances of recovery of function are reasonable. The growth rate of an axon has been estimated to be 2 to 4 mm per day.

Ganglia

The ganglia are aggregations of cell bodies of neurons located outside the CNS. There are two types of ganglia - sensory and autonomic. Sensory (dorsal root, spinal) ganglia. Sensory ganglia lie along the vertebral column by the spine (fig.3), contain pseudounipolar cell bodies of sensory neurons.

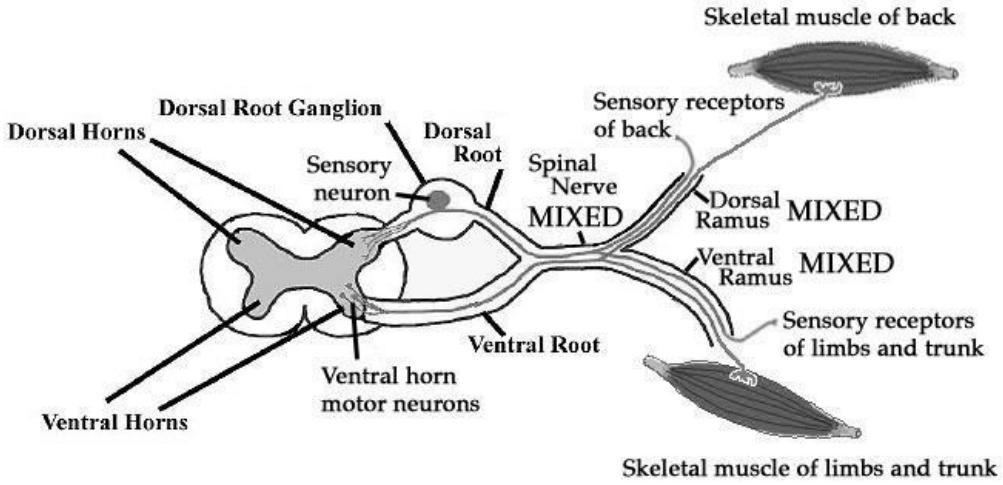


Figure 3. Location of sensory (dorsal root) ganglia.

Sensory ganglia *(***Dorsal Root Ganglion)** of the spinal nerves are called dorsal root ganglia or spinal ganglia. Ganglia associated with cranial nerves are called cranial ganglia. Each spinal ganglion has a thin connective tissue capsule within which the nerve cel are peripherally placed (fig. 4). Ganglion cells will typically be several times larger than other cells in the ganglia. The perikaryon is very large and surrounds a large and light nucleus. Only the cells immediately surrounding the ganglion cells as one flattened layer are satellite cells. With a lot of luck you may see the process of a ganglion cell as it passes out of the capsule of satellite cells.

The dorsal root ganglion contains the cell bodies of sensory neurons that bring information from the periphery to the spinal cord. These neurons are pseudounipolar and contain an axon-like process that bifurcates with one branch extending toward the periphery and the other branch heading toward the grey matter of the spinal cord. Fibers heading toward the periphery leave the ganglion through the spinal nerve, where they run together with motor fibers. Fibers leading to the spinal cord travel through the dorsal root.

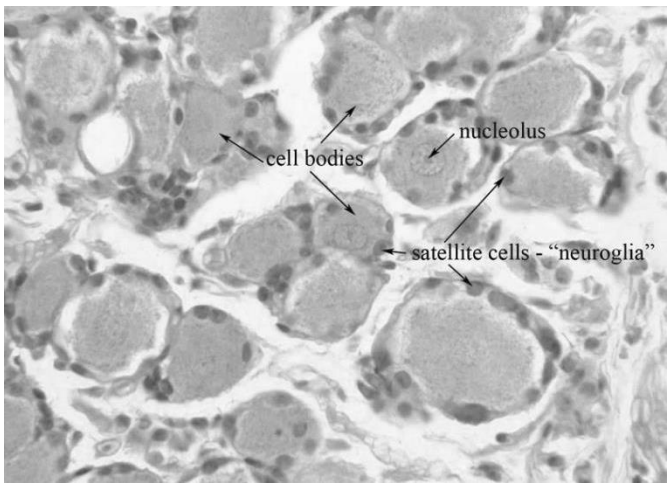


Figure 4. Photomicrograph of sensory ganglion.

Autonomic Nervous System

The autonomic nervous system controls the insides of the body: the viscera or gut. It carries information about the inside of the body to the CNS and controls the action of internal organs, including the gut, the heart, the secretion of epinephrine (adrenalin) and norepinephrine (noradrenalin) from the medulla (middle part) of the adrenal gland, etc. The autonomic nervous system plays an essential role in keeping the body's internal environment (temperature, salt concentration, blood sugar, oxygen and carbon dioxide level in blood, etc) in proper balance, a condition called homeostasis. The autonomic nervous system also plays a major part in emotional experience and expression. When you are emotionally excited, the body shows many changes: blood pressure and heart beat increase, mouth is often dry, stomach has "butterflies" in it. These and other body actions are controlled by the autonomic nervous system.The autonomic nervous system also has two divisions: the **sympathetic** division and the **parasympathetic** division. These two divisions have antagonistic (opposing) effects on the internal organs they innervate (send nerves to = act on). The sympathetic division, shown at the left, is the emergency system. It prepares the body to put out energy and to protect it from effects of injury. It shuts the gut down, speeds up the heart, increases blood pressure, dilates (makes bigger) the pupils of the eyes, makes more glucose (blood sugar) available in the blood for energy, etc. Cannon described these reactions as preparation for fight or flight (running away).The parasympathetic division, shown at the right, is the "housekeeping" division. It acts to replace and recover from the activities of living. Its action is (almost always) the opposite of the sympathetic division. It activates the gut for digestion, slows the heart rate, decreases the blood pressure, etc.

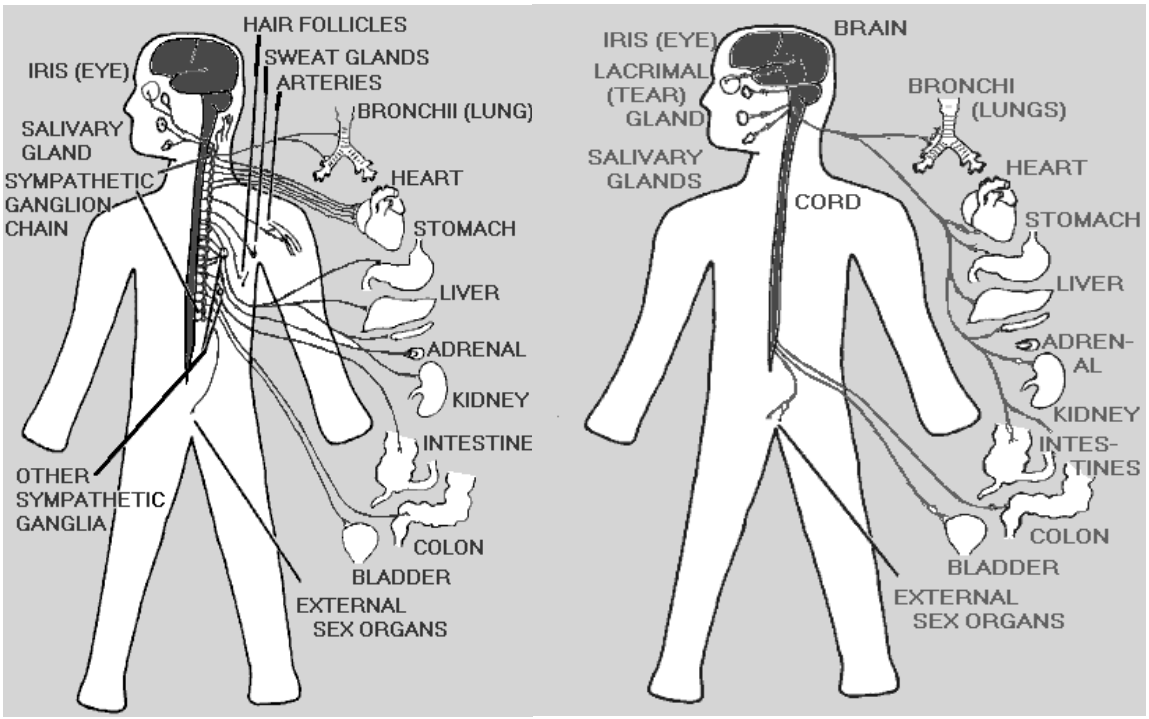


Figure 5. Location of autonomic nervous ganglia.

Centers of the sympathetic part of the autonomic nervous system are located in the chest and transverse segments of the spinal cord (from 1 chest to I - IV lumbar). In the lateral horns of the gray matter of the spinal cord lie the body of the neurons, the axons of which come from the spinal cord located in the anterior part of the root and form separate branches directed toward the sympathetic trunk. Each sympathetic trunk will be a chain of nerve nodes connected to each other. Cute nerves innervate all organs and tissues of the body (pause and increase heart contractions, expand the stars, increase blood pressure, increase metabolism).

The bodies of central parasympathetic neurons are contained in the oblong and medial parts of the brain and the spinal cord. Parasympathetic fibers 7 - 9, 10, 12 cranial nerves are obtained from the medulla oblongata. The main mass of parasympathetic fibers that go from the medulla oblongata leaves it as part of the vagus nerve. Its fibers innervate the organs of the neck, chest, and abdomen. In the spinal cord, parasympathetic nerve centers are located between 2 and 4 sacral segments.

Ganglios of the parasympathetic part of the autonomic nervous system are located in the walls of the internal organs. Intra-organ ganglia are located in the muscular walls of the heart, bronchi, esophagus, stomach, intestines, gall bladder, bladder, and also in the glands of external and internal secretion. The reganglionic fibers of these neurons leave through four of the cranial nerves (III, VII, IX, and X) and also through the II, III, and IV sacral spinal nerves. The **parasympathetic system** is therefore also called the craniosacral division of the autonomic system.

The second neuron of the parasympathetic system is found in ganglia which are always located near or within walls (intramural ganglia) of the effector organs (e.g., stomach, intestines). This ganglia are divided into:

1. submucosal
2. intermuscularis
3. subserosal

The ganglia are surrounded by loose connective tissue **capsule**. Parenchyma of ganglia formed **multipolar neurons** the **cytoplasm of the cell bodies show basophilia** due to **high concentrations of Nissl substance**, while the **nuclei lie eccentrically** with prominent nucleoli. This neurons divided on three types:

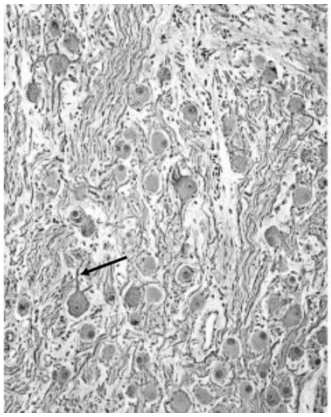
1.Dogiel I – has long axon **- motor neurons**

2.Dogiel II - has the same length of axon and dendrite – **associative neurons**

3. Dogiel III – has long dendrite – **receptor (sensory) neurons**

The ganglia includes preganglionic fibers, they are long and myelinated, and the postganglionic fibers emerging from the ganglion are short and unmyelinated. The neurons of autonomic ganglia are enveloped by a layer of satellite glial cells. Most internal organs have double innervation: each of them comes up with 2 nerves - sympathetic and parasympathetic. A sympathetic part of the autonomic nervous system contributes to the intensive activity of the body, especially in extreme conditions, when a force is required. The parasympathetic part of the autonomic nervous system contributes to the restoration of the organism's lost resources, provides the normal life of the human body in a state of rest and during sleep (slows down the reduction of the heart and reduces their strength, narrows the pupils, reduces blood pressure).

The nuclei of the **sympathetic system** are in the thoracic and lumbar segments (Ti - L|) of the spinal cord. Therefore, the sympathetic system is also called the thoracolumbar division of the autonomic nervous system. The axons of these neurons - preganglionic fibers - leave the central nervous system by way of the ventral roots to join the spinal nerve. After a short distance, the fibers leave the peripheral nerve, via 250white rami communicates, to enter one of the sympathetic chain ganglia, adjacent to the spinal cord, or the collateral ganglia, along the abdominal aorta in the abdomen.In terms of the histology, this type of peripheral ganglia contains cell bodies of postganglionic **multipolar neurons**. On H&E staining most ganglia appear pale and foamy due to the presence of myelinated nerve fibers which wash away during the staining procedure. Mean while the **cytoplasm of the cell bodies show basophilia** due to **high concentrations of Nissl substance**, while the **nuclei lie eccentrically** with prominent nucleoli. The neurons of autonomic ganglia are enveloped by a layer of satellite glial cells.



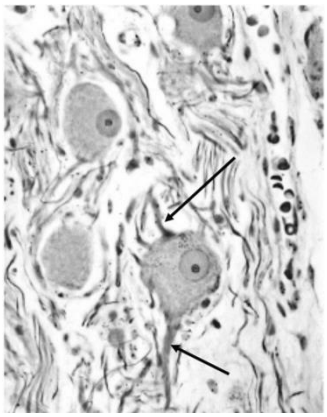


Figure 6. Autonomic ganglion.

The autonomic reflex arc consists of such components (fig.7):

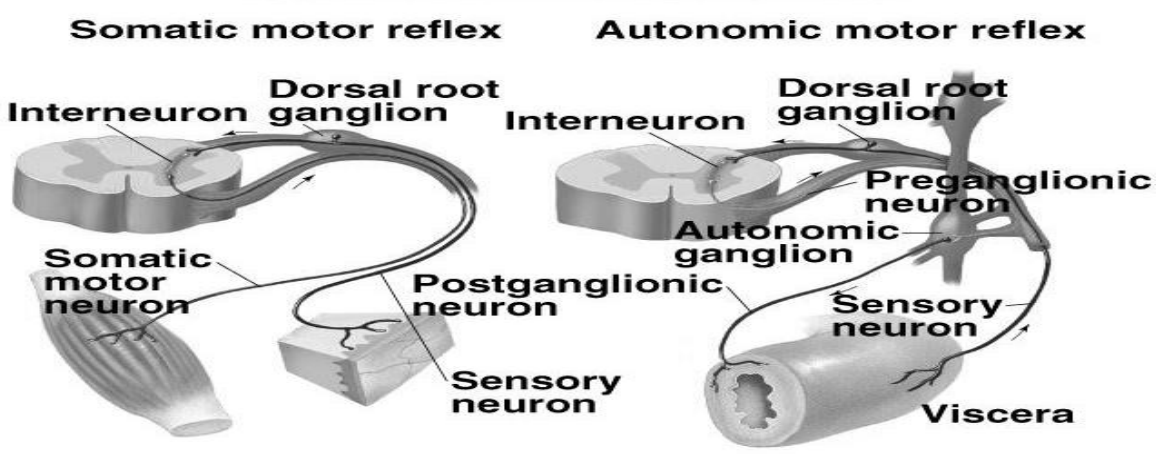


Figure 7. Schematic representation of the autonomic reflex arc.

I. **Receptor part**, as well as in a somatic reflex arc, is formed by afferent pseudounipolar neurons. Their cell bodies settle down in spinal ganglia; however dendrites of these cells form nerve terminations in the internal organs, vessels and glands. Their axons enter a spinal cord in composition of dorsal roots and form synapses on cell bodies and dendrites of interneurons of lateral horns of gray matter.

II. **Associative part** is submitted multipolar interneuron Their dendrites and cell bodies are in lateral horns of a spinal cord. Axons (preganglionic fibers) leave a spinal cord in composition of ventral roots and terminate on dendrites and cell bodies of effector neurones of autonomic ganglia.

III. **Effector part** is formed by multipolar neurons Their cell bodies are in autonomic ganglia, and axons (postganglionic fibers) terminate in the smooth muscles, glands, and heart.

Organization of the central nervous system.

The central nervous system consists **of spinal cord, cerebellum, and cerebrum**. The section of CNS shows regions of white (white matter) and grey (grey matter).

The **white matter** contains myelinated axons and the myelin- producing oligodendrocytes.

The **grey matter** consists of neuronal cell bodies, dendrites, the initial unmyelinated portions of axons and glial cells. The grey matter is prevalent at the surface of the cerebrum and cerebellum, forming the cortex.

White matter is present in more central regions. Aggregates of neuronal cell bodies forming islands of grey matter are called nuclei. Spinal cord In spinal cord the grey matter is central and the white matter is peripheral. The grey matter has the shape of an H (fig. 7)

The **gray matter** is subdivided into horns.

Anterior (ventral) horns are short, broad, directed forwards. Anterior horns contain motor neurons whose axons make up the ventral roots of the spinal nerves.

Posterior (dorsal) horns are narrow, elongated directed backwards. They receive sensory fibers from neurons in the spinal ganglia (dorsal roots) and contain cell bodies of small multipolar interneurons.

Lateral horns (in T2 to Lt segments) contain small motor cells and give rise to preganglionic sympathetic fibers.

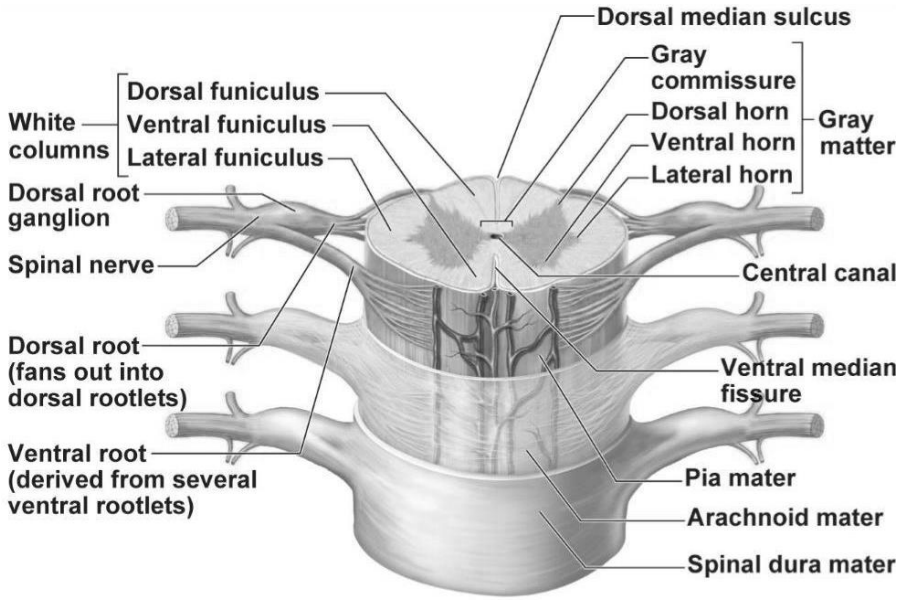


Figure 8. Spinal cord.

Spinal cord cytoarchitectonic. Depending on topography of axons spinal cord neurones are divided on:

1) radicular neurones, which axons form ventral roots;

2) internal neurones, which processes come to an end within of grey matter of the spinal cord;

3) fascicular neurones, which processes form bundles of nerve fibers in white matter of the spinal cord.

The posterior horns contain some nuclei, formed by small multipolar interneurons. These neurons receive sensory' fibers from pseudounipolar neurons of the spinal ganglia (dorsal roots) and also fibers of descending paths from centers lying above (supraspinal centers). Posterior horns consist of dorsomarginal layer, substantia gelatinosa, nucleus proprius, and dorsal nucleus of Clarke. The anterior horns contain the largest (100-150 pm) multipolar motoneurons. Motoneurons are aggregated in nuclei (anterolateral, anteromedial, posterolateral, retroposterolateral, and rosteromedial, central). Its axons form ventral roots. The medial group of motoneurons is developed for spinal cord and innervates the muscles of a trunk. The lateral group is in the region of cervical and lumbar enlargements and innervates the muscles of limbs. The lateral horns are well expressed at the level of thoracic and sacral segments of spinal cord; they contain sympathetic and parasympathetic nuclei of autonomic nervous system.

Glial cells of the spinal cord. The central canal of spinal cord is covered by ependymal cells. Fibrous astrocytes are located in the white matter; protoplasmic astrocytes are found in the grey matter. Oligodendrocytes form the myelin sheathes of nerve fibers. **Microglia** are phagocytic cells, are found in the white and grey

matter.White matter consists of bundles of myelinated nerve fibers forming ascending and descending paths. Each half of white matter is divided into anterior, lateral and posterior regions (funiculi).

Reflex arc. Reflex arcs underlie of activity of nervous system. In reflex arcs the neurones are connected with each other by synapses, form three parts:

- **receptor (afferent),**
- **efferent and posed between them**
- **associative** which in the elementary variant of an arc can be absent.

The receptor part is formed by afferent pseudo unipolar neurons which cell bodies are in spinal ganglia. Dendrites of these cells form nerve terminations in a skin. Axons enter a spinal cord in composition of dorsal roots and form synapses on cell bodies and dendrites of interneurons of posterior horns of its grey matter. The associative part is submitted by multipolar interneurons. Their dendrites and cell bodies are in posterior horns of a spinal cord and axons terminate on cell bodies and dendrites of effector motoneurons of anterior horns of spinal cord. The effector part is formed by multipolar motoneurons. Their bodies and dendrites are in anterior horns. Their axons leave a spinal cord in composition of ventral roots and terminate in skeletal muscles.

Cerebellum

Cerebellum consists of:

1.surface layer of grey matter - cerebellar cortex (fig. 9);

2.central core of white matter (arbour vitae);

3. cerebellar nuclei embedded in the white matterCerebellar cortex is responsible for maintaining balance and equilibrium, muscle tone, and coordination of skeletal muscles.

The cerebellar cortex is divided into three layers (fig. 10,11):

1. Outer **molecular layer** which contains superficially located stellate cells, basket cells, and the dendrites of Purkinje cells and the axons of granule cells but few cell bodies.

2. **Middle Purkinje cell** layer which contains a single layer of large, flask-shaped Purkinje cells (fig.9). Their dendrites project into the molecular layer, and their myelinated axons project into the white matter. Each Purkinje cell receives hundreds of thousands of excitatory and inhibitory synapses that it must integrate to form the proper response. Purkinje neurons have a broad dendritic tree with its width oriented perpendicular to the long axis of the folium. The Purkinje cell is the only cell of the cerebellar cortex that sends information to the outside.

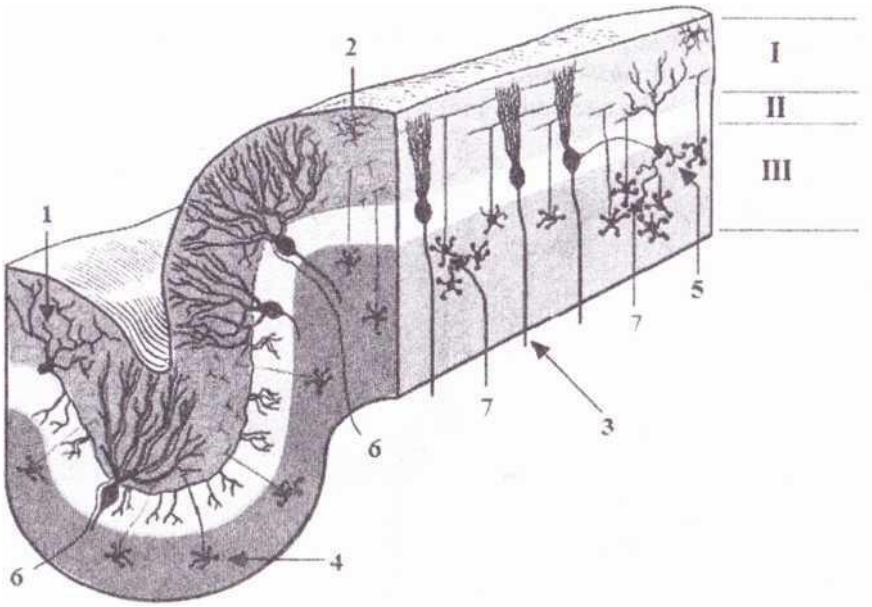


Figure 9. Schematic diagram of cerebellar cortex. I - molecular layer: 1 - basket cell, 2 - stellate cell; II - Purkinje cell layer: 3 - Purkinje cell; III - granule cell layer: 4 - granule cell, 5 - Golgi cell; 6 — climbing fiber, 7 - mossy fiber

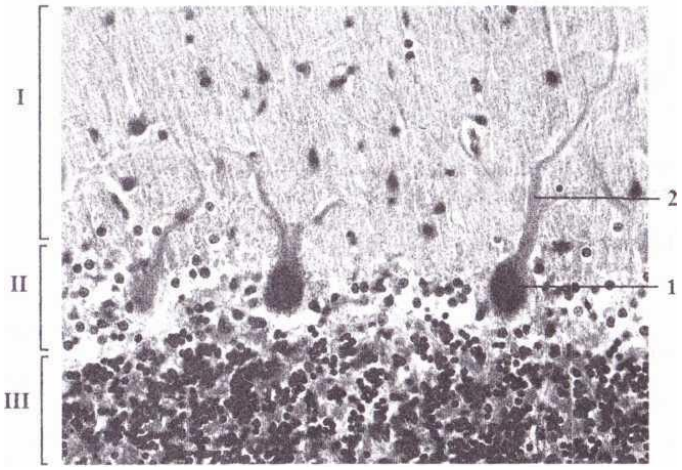


Figure 10. Photomicrograph of the cerebellar cortex. I - molecular layer, II - Purkinje cell layer, III - granule cell layer; 1 - Purkinje cell bodies, 2 — Purkinje cell dendrites

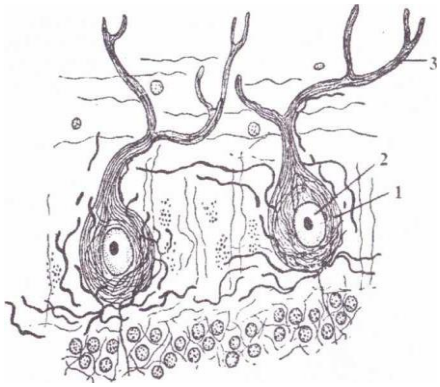


Figure 11. Schematic diagram of Purkinje cells. 1 - Purkinje cell body, 2 - nucleus of Purkinje cell, 3 - dendrites of Purkinje cell

3.Inner **granule cell** layer composed of vast numbers of very small neurons called granule cells and Golgi cells. Each granule cell has a few short dendrites within the granule cell layer. Each granule cell axon projects into the molecular layer and bifurcates into parallel fibers which extend parallel to the long axis of each layer. **Climbing fibers** and mossy fibers enter the cerebellar cortex. Axons of Purkinje neurons leave the cerebellar cortex. Climbing fibers are axons that originate in the inferior olive, ascend through the inferior cerebellar peduncle, and make terminal arborisations that invest the dendritic tree of Purkinje cells. **Mossy fibers** are one of the major inputs to cerebellum. There are many sources of this pathway, the largest of which is the cerebral cortex, which sends input to the cerebellum via the pontocerebellar pathway. Other contributors include the vestibular nerve and nuclei, the spinal cord, the reticular formation, and feedback from deep cerebellar nuclei. Axons enter the cerebellum via the middle and inferior cerebellar peduncles, where some branch to make contact with deep cerebellar nuclei. They ascend into the white matter of the cerebellum, where each axon branches to innervate granule cells in several cerebellar folia.

CEREBRAL CORTEX.

Cerebral cortex The cerebral hemispheres consist of a convoluted cortex of grey matter. Central mass of white matter conveys fibers between different parts of the cortex and to and from other parts of CNS. **Cerebral cortex cytoarchitectonic**.The neurons of the cerebral cortex are arranged in six layers (fig. 12):

I. **Molecular layer is** most superficial, mainly contains dendrites and axons of neurones originating in other layers of cortex; horizontal cells of Cajal. Axons of these cells form tangential plexus.
II. **External granular layer** contains small pyramidal cells and stellate (granular) cells and also various axons and dendrites of neurons from deeper layers.
III. **External pyramidal layer** contains medium-sized pyramidal cells, increasing in size deeper in the layer.
IV. **Internal granular layer** is a thin layer characterized by densely packed stellate and pyramidal celts.
V. **Internal pyramidal (ganglionic) layer** contains large pyramidal cells, and in the motor cortex the giant pyramidal neurons of Betz.
VI. **Multiform layer** consists of cells of various shapes: numerous small pyramidal cells and cells of Martinotti, as well as stellate cells especially superficially, and fusiform cells in the deeper part. Types of cerebral cortex In the certain areas of a cerebral cortex connected to execution of different functions, development of those or its other layers dominates.

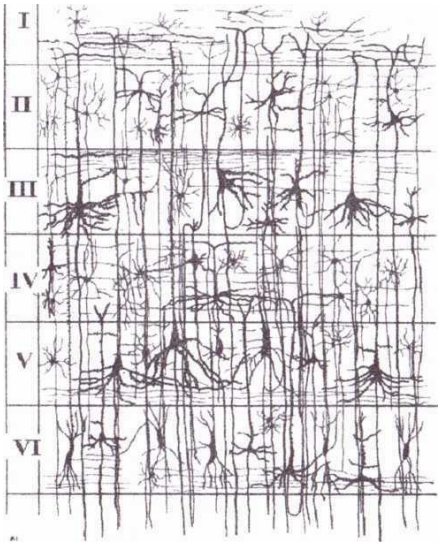


Figure 12. Schematic representation of the cerebral cortex. I — molecular layer, II - outer granular layer, III - pyramidal cell layer, IV - Inner granular layer, V - ganglionic layer, VI - multiform cell layer Therefore the cerebral cortex is divided into granular and agranular. **Agranular type of cerebral cortex** is characterized by the greatest development of III, V and VI layer at weak development of II and IV (granular) layers (motor centers). **Granular type of cerebral cortex** is characterized by weak development of the layers containing pyramidal cells (III, V) at greatest development of granular (II and IV) layers (sensory centers).

Modular principle of the cerebral cortex organization. Modules are structural and functional units of cerebral cortex. They are disposed vertically and have the shape of cylinders in diameter 200-300 microns which are passing upright through all thickness of cortex (fig.14). In cerebral cortex of the person about 2-3 million such columns is present, everyone contains approximately 5000 neurones.

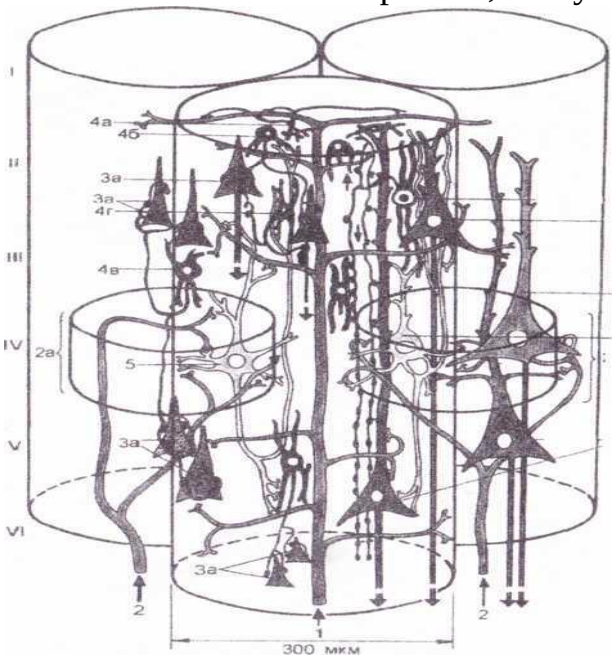


Figure 13. Module of the cerebral

The blood-brain barrier consists of (fig. 16):

1. Endothelial cells of the capillaries connected with each other by tight junctions represent the main structural component of barrier.
2. Basal lamina of the endothelial cells of the capillaries.
3. Perivascular feet of astrocytes, which surround by the blood capillaries. As a result, only certain materials are allowed to pass from blood vessels to the brain. Substances such as O_2, glucose, H_20, CO_2, essential amino aids, and most lipid-soluble substances enter the brain readily. Other substances, such as creatine and urea (wastes transported in the blood), most ions (Na+ , K+ , CF), proteins, and certain toxins either have limited access or are totally blocked from entering the brain. Unfortunately, most antibiotic drugs are equally blocked from entering, while other substances such as caffeine, alcohol, nicotine, and heroin readily enter the brain (because of their lipid solubility).

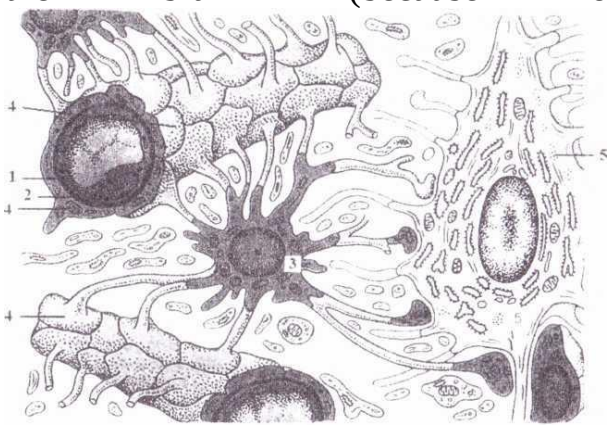


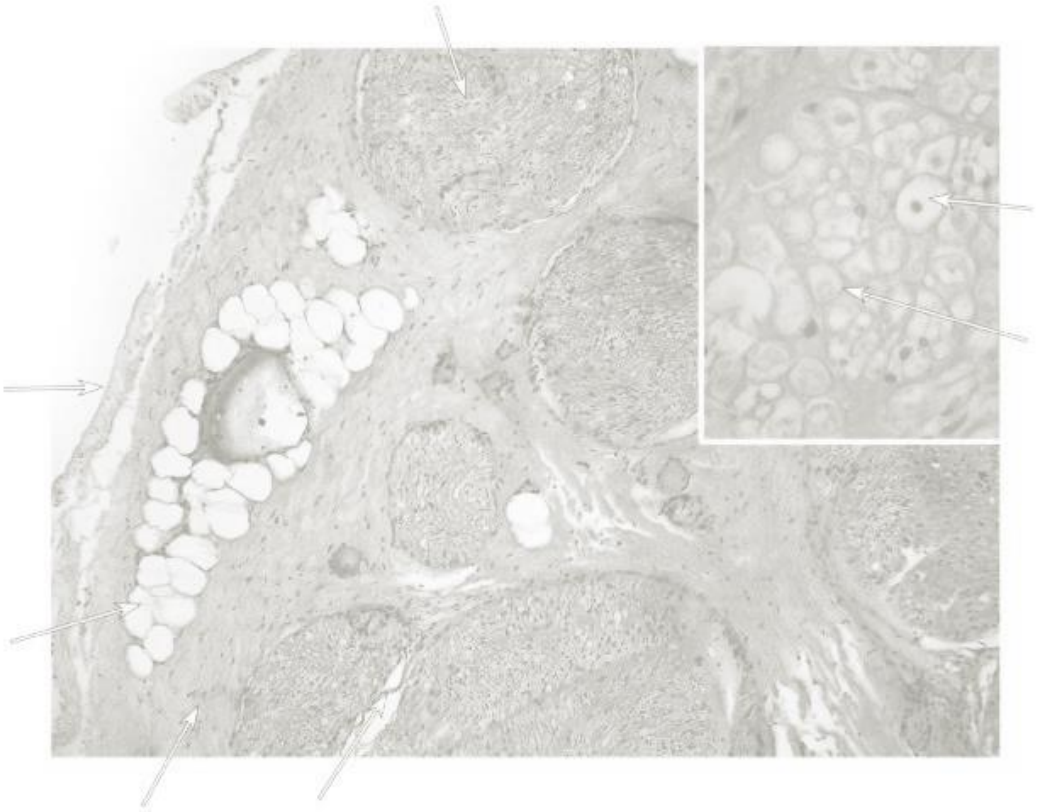
Figure 14. Schematic diagram of the blood-brain barrier. 1 - endothelial cells of blood capillary, 2 - basal lamina of the endothelial cells, 3 - cell body of the astrocyte, 4 — perivascular feet of astrocytes. 5 — neuron

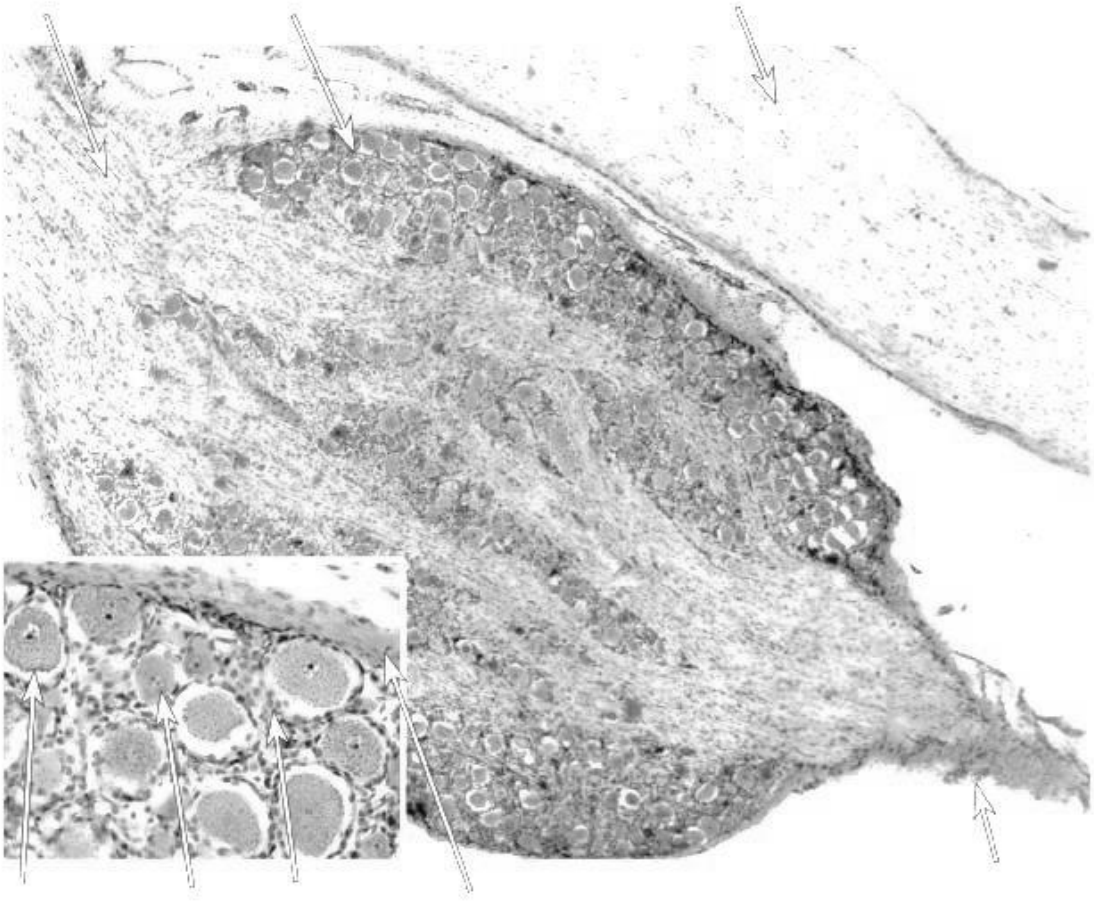
Practical lessons

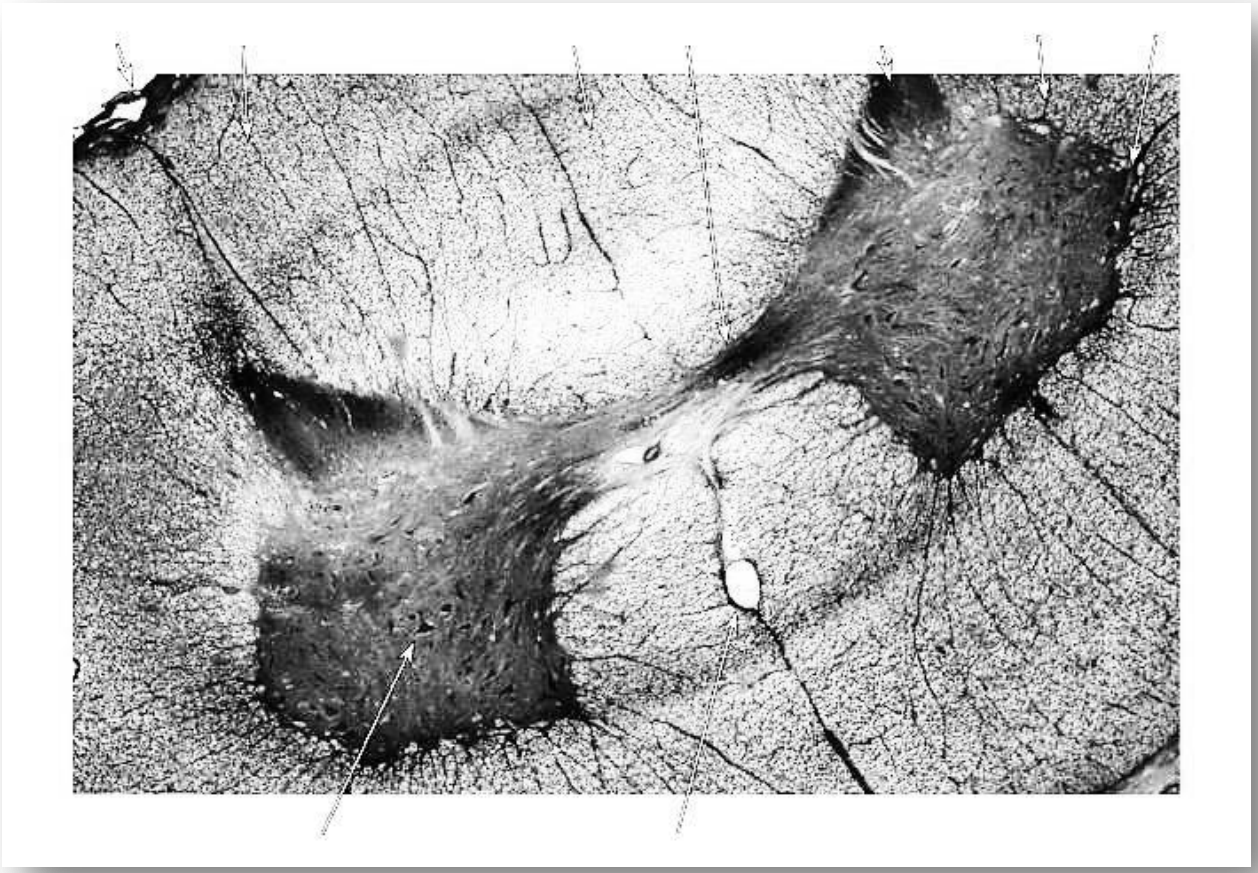
1. Nerve system: general morphofunctional characteristic, classification (structural and functional).
2. Central nerve system, grey and white matter, nerve centres, meningeal layers. Blood-brain barrier.
3. Cerebral cortex. Morphofunctional characteristic, cyto- and myeloarchitectony. Gliocytes of the cortex.
4. Cerebellum: general structure and functions. Cerebellar cortex, neurons. Interneuronal communications. Gliocytes of the cerebellum.
5. Brainstem. Grey matter (neuronal compounds). Medulla oblongata. Reticular formation.
6. Diencephalon. Thalamus and hypothalamus, principle nuclei, functions.
7. Spinal cord: general morphofunctional characteristic. Grey matter (nuclei and their cells compounds). Gliocytes.
8. Peripheral nerve system. Regeneration of nerve after the damage. Simple and complex somatic reflex arc, principal compounds.
9. Morphological and functional peculiarities of spinal node: sensory neurons and neuroglial compounds.

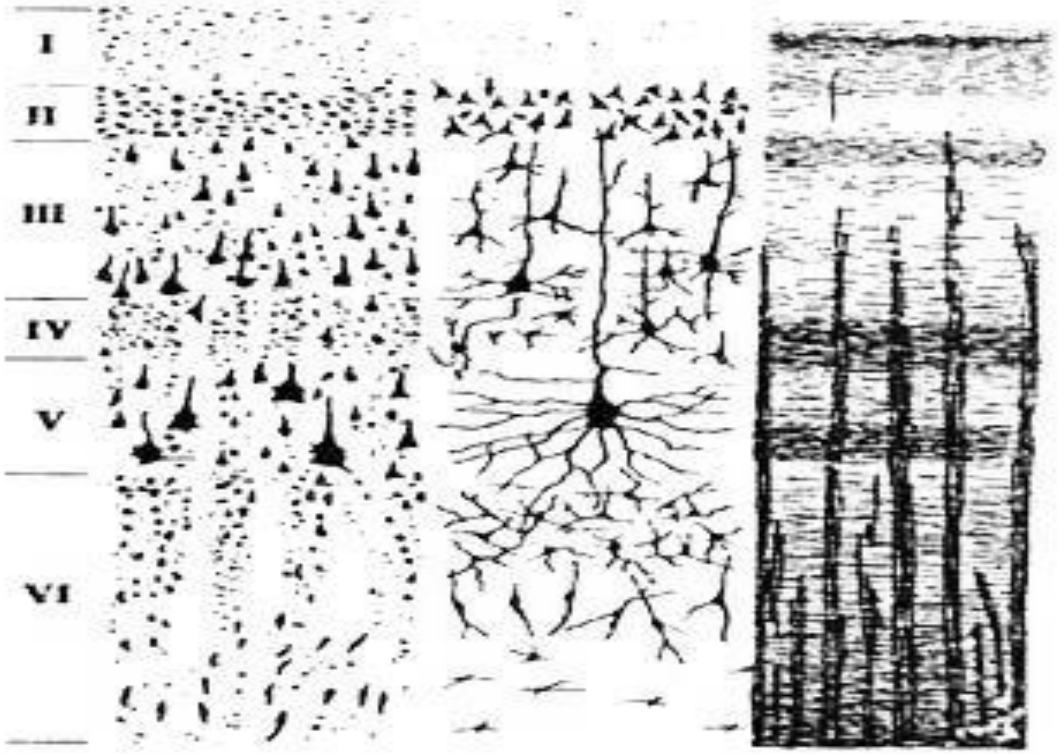
10. Autonomic (vegetative) nerve system: structural peculiarities. Vegetative ganglia: cellular structure and disposition. Reflex arc: special features.

Paint and mark basic histological structure





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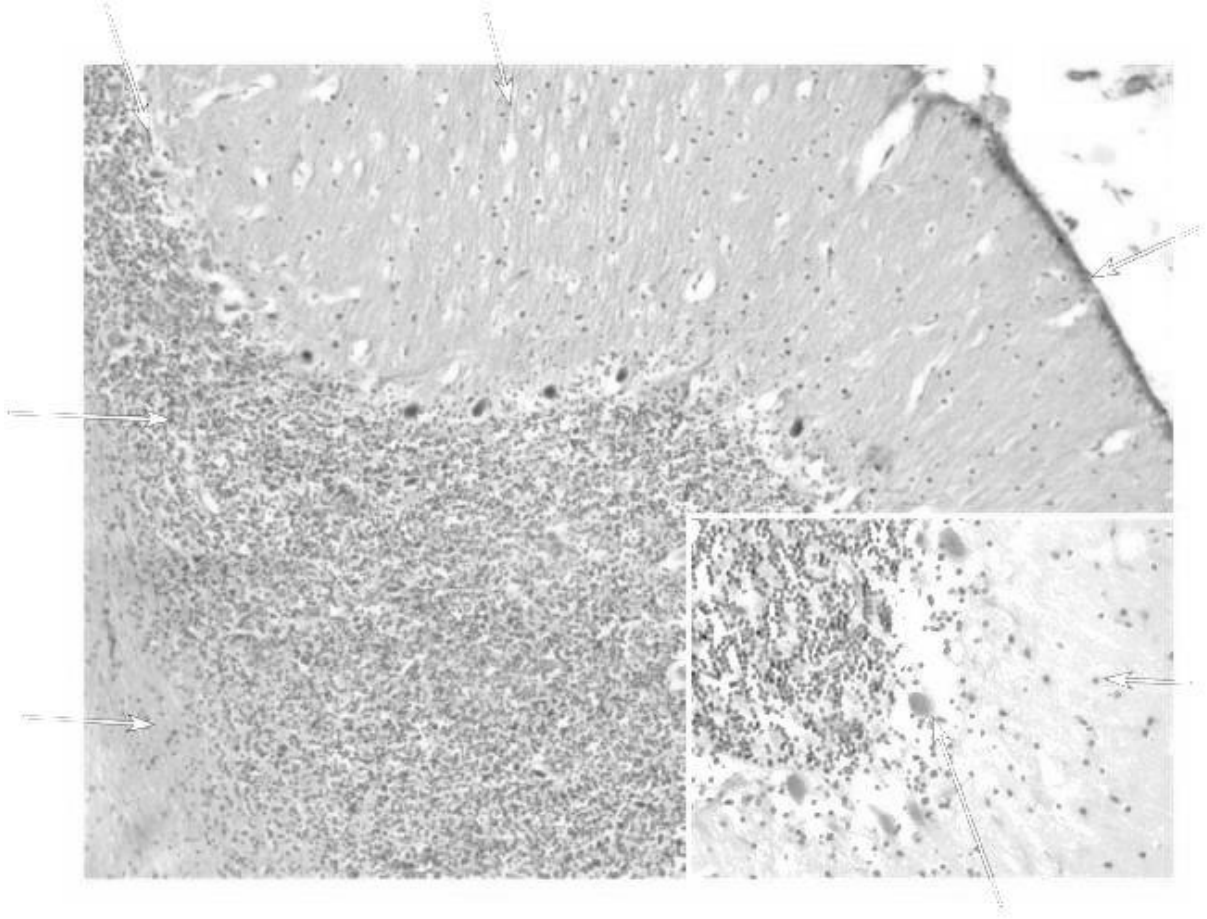
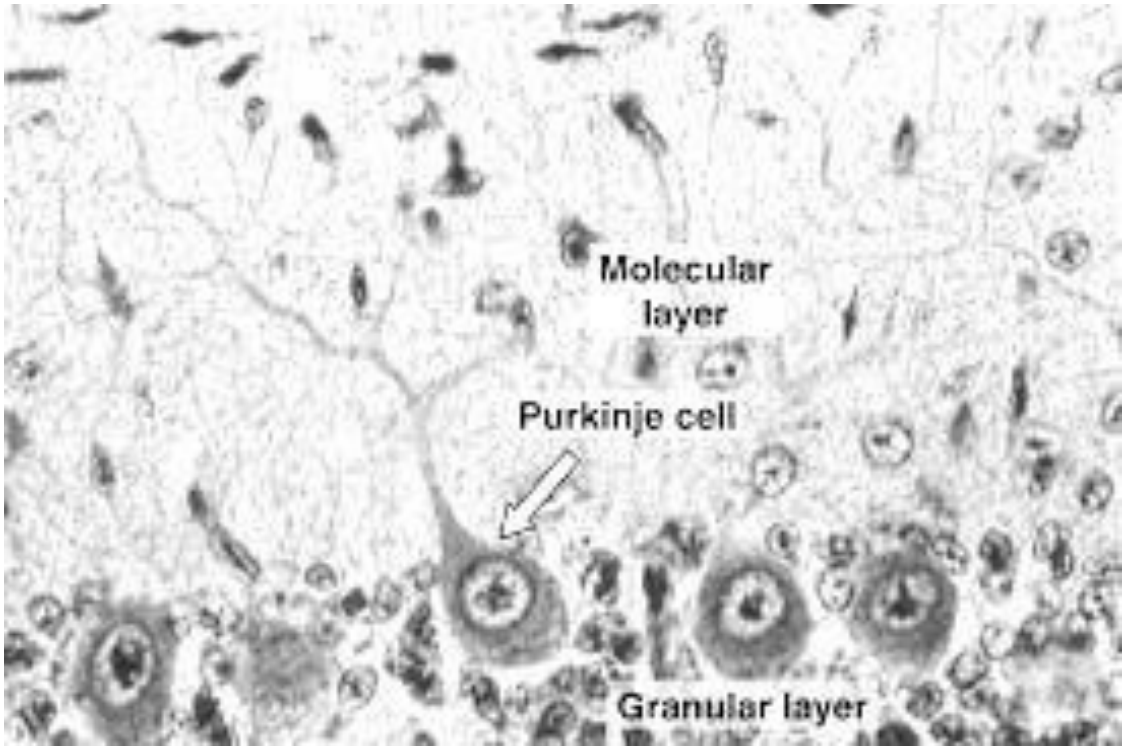




Signature of teacher _____

SENSORY SYSTEM

I. VISION: THE PHOTORECEPTOR SYSTEM

Overv iew of the sensory system The sensory system is a part of the nervous system responsible for processing sensory information. Recognized sensory systems are those for vision, hearing, somatic sensation (touch), taste and olfaction (smell). The senses are transducers from the physical world (heat, pressure, light, sound, etc) to the realm of the mind. The human sensory system consists of the following subsystems:

- visual system;
- auditory system;
- somatosensory system (touch and proprioception) ;
- gustatory system;
- olfactory' system.

Human sensory receptors are:

- chemosensors;
- mechanoreceptors (Pacinian corpuscles, Meissner's corpuscles, Merkel's discs, and Ruffini corpuscles);
- nociceptors; photoreceptors;
- thermoreceptors.

The sensory system consists of:

- **peripheral parts** (sensory receptors),
- **intermediate parts** (neural pathways),
- **central** (parts of the brain involved in sensory perception).

Receptors are subdivided into:

- neuro-sensitive receptors are neurons which accept sensitive signals by the peripheral processes, transduce them to nervous impulses andtransfer in CNS by the central processes. They are part of the photoreceptor system and olfactory organ;
- senso-epithelial receptors are the specialized epithelial cells which accept sensitive signals; the transmission of nervous impulses from them in CNS is carried out due to their connections with the endings of neurons. They are part of the vestibulocochlear apparatus and taste organ.

Photoreceptor system .The photoreceptor system consists of the eyeball and accessory structures (conjunctiva, eyelids, and lachry mal apparatus). Eyeball The eye is complex and highly specialized organ of photoreception, a process which involves the conversion of different, quanta of light energy into nerve action potential. The eyeball is composed of 3 layers (fig.15):

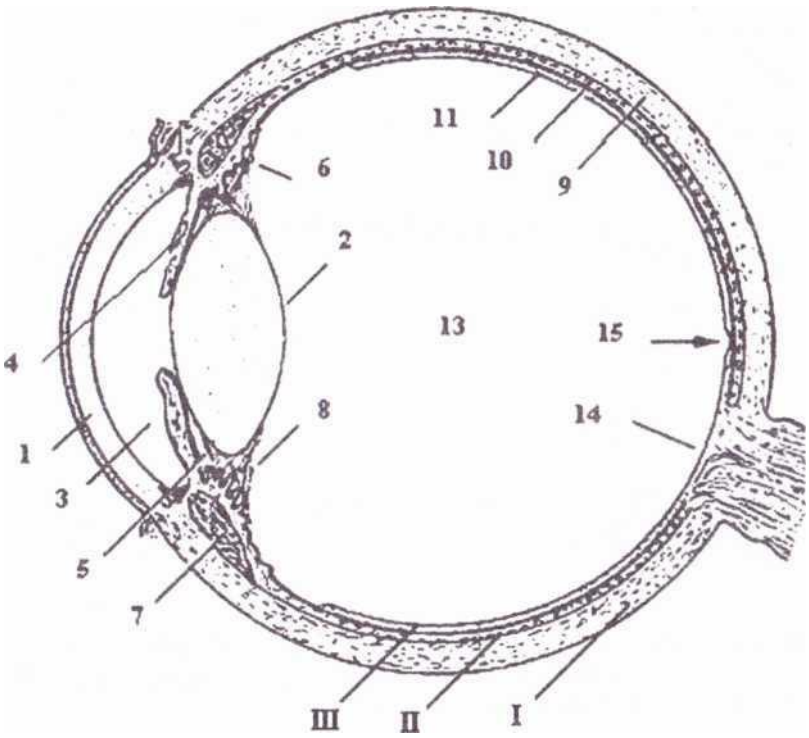


Figure 15. Structure of the eyeball. I - external layer, II — middle layer, III - inner layer, 1 - cornea, 2 - lens, 3 - anterior chamber. 4 - iris, 5 — posterior chamber, 6 — ciliary body, 7 — ciliary muscle, 8 - zonule fiber, 9 — sclera, 10 - choroid, 11 - retina, 12 - optic nerve, 13 - vitreous body, 14 - optic disc, 15 - fovea

- **external layer** (tunica fibrosa) that consists of sclera and cornea,
- **middle layer** (vascular layer or uveal tract) which consists of the choroid, ciliary body, and iris;
- **inner layer** of nerve tissue, which consists of an outer pigment epithelium and an inner retina propria.

The lens of the eye is biconvex transparent structure, which is attached to the ciliary body by the suspensory ligament. Partly covering the anterior surface of the lens is pigmented expansion of the middle layer called iris. The round hole in the middle of the iris is the pupil The eye contains 3 compartments:

- anterior chamber is space between the cornea and the iris and the lens;
- posterior chamber lies between the iris and the lens; y vitreous space.

Both the anterior and posterior chambers contain fluid called aqueous humor. The vitreous space is filled by a gelatinous substance called the vitreous body.

External layer.The external (corneoscleral) layer forms a fibro-elastic capsule which supports the eye. The posterior five-sixths, the sclera, are opaque and provide insertion for the extra-ocular muscles. It consists of dense connective tissue made up of collagen bundles, a moderate amount of ground substance, and a few fibroblasts. The anterior one-sixth, the cornea, is transparent and colourless. **The cornea consists of 5 layers** (fig. 16):

- epithelium,
- anterior elastic lamina (Bowman's membrane),
- stroma.

- posterior elastic lamina (Descemet's membrane),
- endothelium.

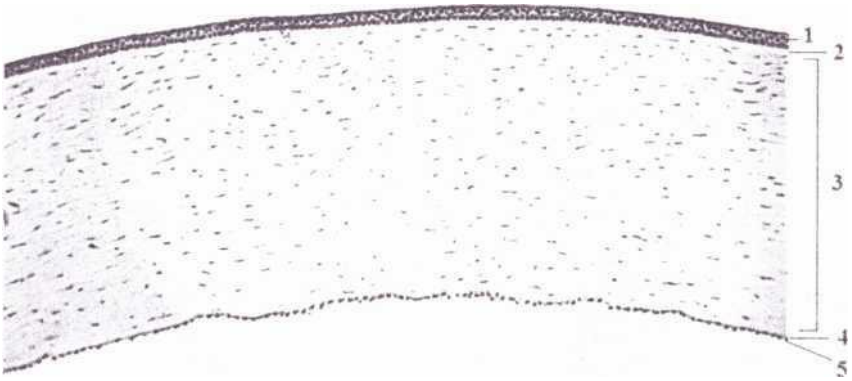


Figure 16. Photomicrograph of cornea. 1 — epithelium, 2 - anterior elastic lamina (Bowman's membrane), 3 - stroma, 4 - posterior elastic lamina (Descemet's membrane), 5 - endothelium Corneal epithelium is stratified squamous non-keratinized, consists of 5-6 layers of cells.

Anterior elastic lamina (Bowman's membrane) is acellular thick homogeneous layer. It consists of densely packed collagen fibrils embedded in ground substance. Stroma forms 90 % of cornea thickness. It consists of 200 - 250 layers of regularly organized collagen fibers. Collagen fibres within each layer will run parallel to each other but at large angles to collagen fibres in the next layer. Flattened fibrocytes are located between the layers of collagen fibres. The regular arrangement of the collagen fibres, their small diameter (20 - 60 nm) and absence of blood vessels result in the transparency of the cornea.

Posterior elastic lamina (Descemefs membrane) is a thick homogeneous structure composed of collagen fibers, intercellular matrix, and no cells. Endothelium is simple squamous epithelium.

The **corneo-scleral junction** is known as the limbus. In the region of the limbus in the stromal layer, irregular endothelium-lined channels, the trabecular meshwork, merge to form the canal of Schlemm, which drains fluid from the anterior chamber of the eye. The canal of Schlemm communicates externally with the venous system.

Middle layer (vascular layer or uveal tract) The middle layer consists of 3 components:

- choroid,
- ciliary body,
- iris.

Choroid.Choroid lies in the posterior five-sixths of the eye and contains:

- suprachoroidal lamina (the outer layer) is a layer of loose connective tissue rich in melanocytes;
- vascular lamina contains arteries and veins;
- choriocapillary lamina (the inner layer) is rich in small vessels. It has an important function in nutrition of the retina;

- basal (Bruch's) lamina separates the choriocapillary lamina from the retina. It consists of elastic and collagen fibers that are covered by the basal lamina of the capillaries of choriocapillary layer on one side and the basal lamina of the pigment epithelium on the other side.

Ciliary body.The ciliary body, an anterior expansion of the choroid at the level of the lens, thickened ring that lies at the inner surface of the anterior of the sclera. It forms a triangle in transverse section (fig. 17).

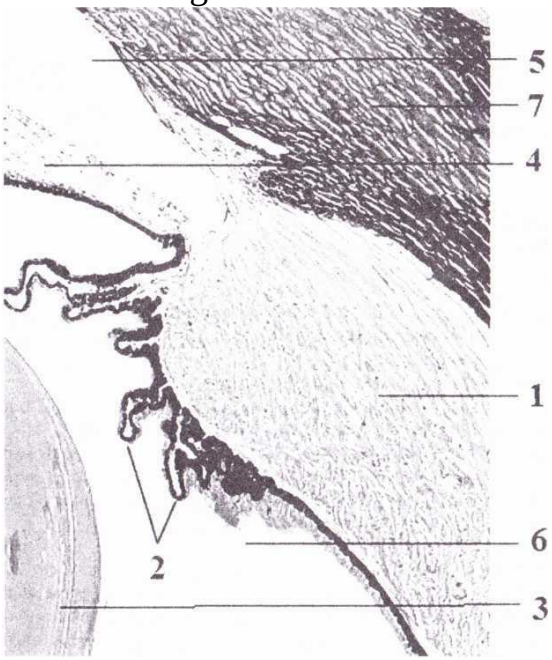


Figure 17. Eye (anterior lateral portion). 1 - ciliary body, 2 - ciliary processes, 3 - lens, 4 — iris, 5 - anterior posterior chamber, 6 — posterior chamber, 7 — sclera

Ciliary body contains:

- **ciliary muscle** is important in visual accommodation.
- **ciliary processes** are extensions of the ciliary body.

They are the place of attachment of zonule fibers that insert into the capsule of the lens and anchor it. Ciliary processes are covered by epithelium. The cells of this epithelium secrete aqueous humor into the posterior chamber.

Iris. The iris is an extension of the choroid in front of the lens. The aperture of the iris is called the pupil. The iris contains the dilator pupillae muscle and sphincter pupillae muscle which are formed by smooth muscle tissue.

The iris consists of 3 layers:

- **anterior epithelium** contains of pigment cells and fibroblasts;
- **intermediate layer** contains loose connective tissue rich in blood vessels, pigment cells;
- **posterior epithelium** consists of 2 layers of columnar cells. The highly pigmented iris acts as an adjustable diaphragm with regulates the amount of light reaching the retina.

Lens .The lens is a transparent, colourless, plastic and biconvex disk which is kept by zonule fibers. The lens changes its curvature in dependence on tension of the zonule fibers and providing thus ability to focusing on a retina the subjects posed on various distance from an eye. **The lens has 3 principal components** (fig. 18):

- lens capsule,
- subcapsular epithelium,
- lens fibers.

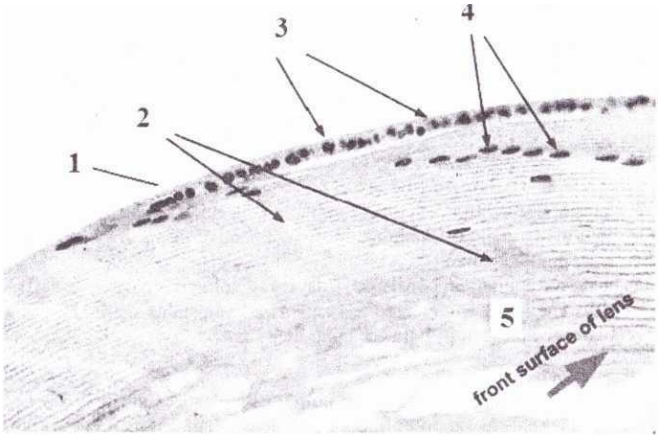


Figure 18. Photomicrograph of the lens. 1 - lens capsule, 2 - subcapsular epithelium, 3 — lens fibers, 4 - nuclei of the lens fibers, 5 - nucleus of lens

1**. Lens capsule** is the thick homogeneous layer covering the lens outside, which contains glycoproteins and the network of microfilaments. It is a basement membrane of lens epithelium, serves as a place of attachment of zonule fibers.

2. **Subcapsular epithelium** consists of a single layer of cuboidal epithelial cells that are present only on the anterior surface of the lens.

3. **Lens fibers** are elongated and appear as thin flattened structures. They are highly differentiated cells derived from cells of the subcapsular epithelium. They eventually lose their nuclei and other organelles and become greatly elongated fibers. These cells are filled with proteins called crystalline.

The lens is held in place by a radially oriented group of fibers, the zonule, which inserts on one side on the lens capsule and on the other on the ciliary' body. Zonular fibers are similar to the microfibrils of elastic fibers. This system is important in the process known as accommodation, which permits focusing on near and far objects by changing the curvature of the lens. When the eye is at rest or gazing at distant objects, the lens is kept stretched by the zonule in a plane perpendicular to the optical axis. To focus on a near object, the ciliary muscles contract, causing forward displacement of the choroid and ciliary body. The tension exerted by the zonule is relieved, and the lens becomes thicker, keeping the object in focus.

Vitreous body .The vitreous body occupies the region of the eye behind the lens. It is a transparent gel that consists of water (about 99%), collagen, and hyaluronic acid. The vitreous body supports the lens and retina.

Retina. The retina, the inner layer of the globe, consists of two portions:

- **posterior (optic) part** lines the inner surface of the eye posterior to the ora serrata, is photosensitive;
- **anterior (nonvisual) part** lines the inner aspect of the ciliary body and the posterior surface of the iris, located anterior to the ora serrata.

The structural components of retina are: 1) pigment epithelium, 2) supporting cells, 3) neurons. 1. The **retinal pigment epithelium** (fig. 19) shows a dark colouration due to the abundant melanin within the cell. Pigment cells are cuboidal or columnar cells, which form a single layer,within the cell.

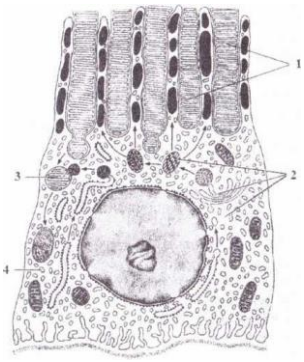


Figure 19. Schematic diagram of the retinal pigment cell. 1 - apical portions of photoreceptors, 2 - synthesis of melanin, 3 — lysosomes, 4 - vitamin A (from Junqueira L.C. and Carneiro J., 2005)

This dark pigment functions to absorb light that has already passed through the retina and did not interact with the photoreceptors. In this way, this dark layer reduces scatter by preventing light from bouncing around inside the eye, thus reducing interferences that would cause a distorted image to be formed. The cells of the pigment epithelium have lysosomes containing enzymes that digest phagocytised parts of the apical portion of photoreceptors that are continually shed.

2. **Supporting (Muller's) cells** or retinal gliocytes are elongated cell extending through all thickness of the retina perpendicularly to its layers, are analogous to the neuroglia of the CNS. Muller's cells provide structural support and may also mediate the transfer of essential metabolites such as glucose to the retinal neurones.

3.Neurones of a retina form three-part chain of radially posed cells, connected with each other by synapses (fig. 20):

- **Photosensitive cells** (the rods and cones);
- **Bipolar neurons,** which connect the rods and cones to the ganglion cells; **Multipolar** ganglion cells, which axons converge at the optic papilla, forming the optic nerve Photosensitive cells
- Rod cells are thin, elongated, cylindrical, bipolar cells consist inner and outer segments, a nuclear region, and a synaptic region (fig.24). The outer segment is separated from the inner segment by a constriction (cilium). The outer segment is composed of numerous flattened membranous discs, which are not continuous with the plasma membrane. These discs contain visual purple rhodopsin. The inner segment contains mitochondria, smooth and rough endoplasmic reticulum, polyribosomes. Nucleus lies near the center of the inner segment. Rod cells are found in peripheral parts of the retina, accept light signals of low intensity (twilight vision) and responsible for black-and-white vision. Human retina has 120 million rod cells.

- Cone cells are also elongated neurons but somewhat shorter and wider than rods. The structure of the cones is similar to that of the rods: the cone contains outer and inner segments, which are separated by cilium. Inner segment contains ellipsoid, which consists of lipid droplet and accumulation of mitochondria. The cones differ from the rods in their form (conical) and the structure of their outer segments. This region is also composed of stacked membranous disks; however, they are not independent of the outer plasma membrane but arise as invaginations of this structure (fig.24). These discs contain visual purple iodopsin.

Because humans usually have three kinds of cones with different photopsins, which have different response curves and thus respond to variation in colour in different ways (in the red, green, or blue region of the visible spectrum), they have trichromatic vision. Cone cells are found in the central parts of the retina and are especially numerous in the fovea of a macula lutea, in which retina has the maximum photoreceptor sensitivity. They react to light of high intensity, provide diurnal and colour vision. Human retina has 6-7 million cone cells.

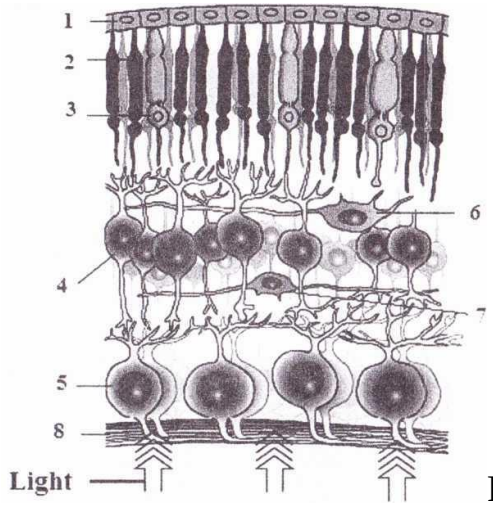


Figure 20. Schematic drawing of the retinal neurons. 1 — retinal pigment epithelium, 2 - rod cell, 3 - cone cell, 4 - bipolar cell, 5 — ganglion cell, 6 - horizontal cell, 7 - amacrine cell, 8 - optic nerve.

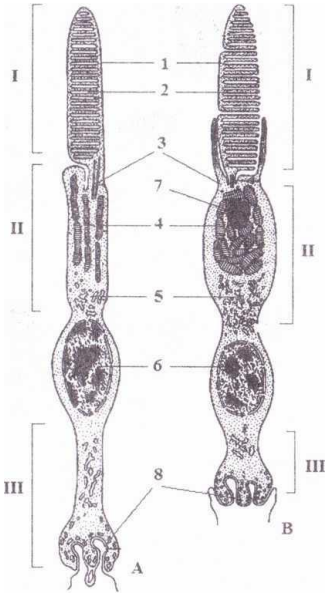


Figure 21. Schematic diagram of the photoreceptors. A - rod cell, B — cone cell, I — outer segment, II — inner segment, III - synaptic region; 1 — plasmolemma, 2 - membranous discs, 3 - cilium, 4 — mitochondria, 5 - Golgi complex, 6 — nucleus, 7 - ellipsoid, 8 - synapse

Bipolar (associative) cells are connected by dendrites to axons of photosensitive cells, and their axons transfer nervous impulses to dendrites of ganglion cells.

Ganglion cells are typical multipolar nerve cells.

Dendrites form connections with axons of bipolar cells. Axons, collecting together, form an optic nerve. Association neurons of retina (fig. 20)

1. **Horizontal** cells are associative multipolar neurons. They establish contact between different photoreceptors. It is possible that they act to integrate stimuli

2. **Amacrine** cells establish contact between the ganglion cells. The retinal layers 10 layers of the retina from outside are (fig.22):

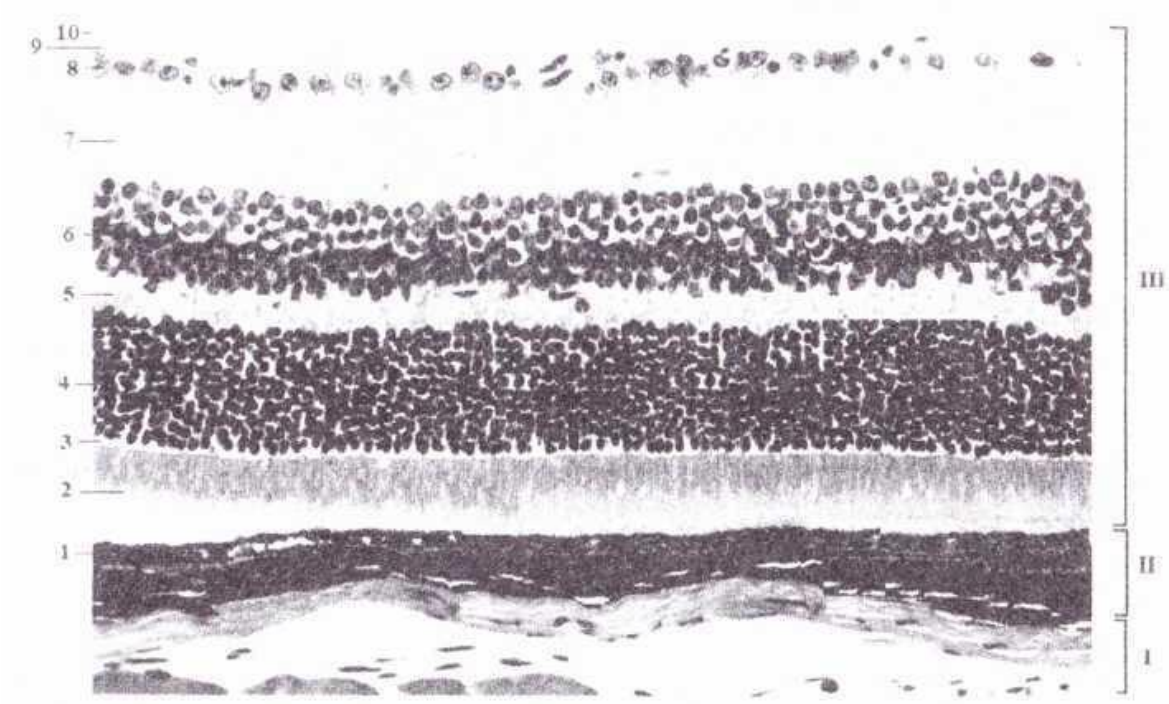


Figure 22. Photomicrograph of the human retina. I - sclera, II — choroid, III — retina: 1- retinal pigment epithelium, 2 — photosensitive layer (outer segments of rods and cones), 3 - outer limiting membrane, 4 - outer nuclear layer, 5 - outer plexiform layer, 6 - inner nuclear layer, 7 - inner plexiform layer, 8 - ganglion cells layer, 9 - layer of afferent fibers, 10 - inner limiting membrane

- **pigment epithelium** is a single layer, resting on Bruch's membrane which separated them from the choroid;
- **photosensitive** layer are the outer processes of the photoreceptor cells (rods and cones);
- **outer limiting membrane** formed by the outer ends of Muller's cells;
- **outer nuclear layer** contains cell bodies of rods and cones;
- **outer plexiform** layer is synaptic connections between the axons of the rods and cones and the dendrites of bipolar cells;

- **inner nuclear layer** contains cell bodies of bipolar, horizontal and amacrine cells; - inner plexiform layer is synaptic connections between the axons of the bipolar cells and the dendrites of multipolar ganglion cells;
- **ganglion celI layer** contains the cell bodies of ganglion ceils;
- **layer optic nerve fibers** contains the axons of ganglion cells, which collecting together, form an optic nerve;
- **inner limiting membrane** is formed by the inner ends of the Muller's cells.

The retina has two zones with **special structural and functional** characteristics.

1. Fovea is a conical depression at the posterior pole of the optical axis (fig. 26).

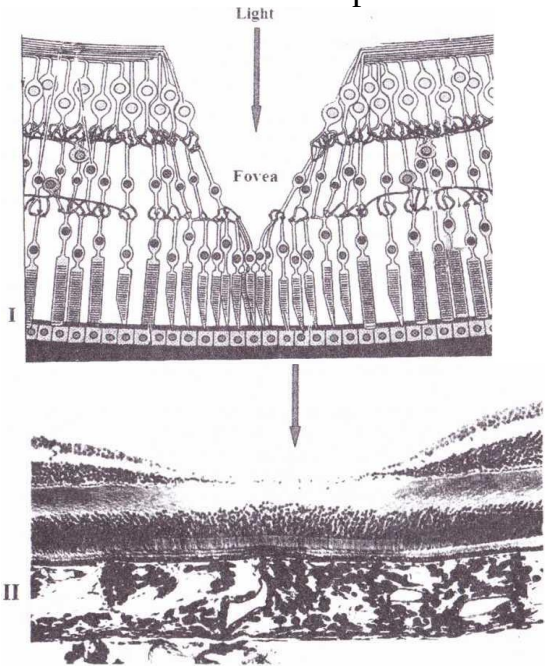


Figure 23. Fovea. I - schematic diagram, II - photomicrograph

In the fovea (0,5 mm in diameter) retina is very7 thin because the bipolar and ganglion cells accumulate in the periphery of this depression. In this area retina consists only of cone cells, and blood vessels are absent. Surround the fovea is an ovoid ye llow area called the macula lutea (1-2 mm in diameter). Light falls directly on the cones in the fovea. In this area the retina has the maximum photoreceptor sensitivity.

2. The afferent fibers from the retina converge at appoint medial to the fovea, the optic papilla or optic disc (fig.27).

The fibers then penetrate the sclera to form the optic nerve. Rods and cones are absent here. Optic disc is insensitive to light and is termed the blind spot.

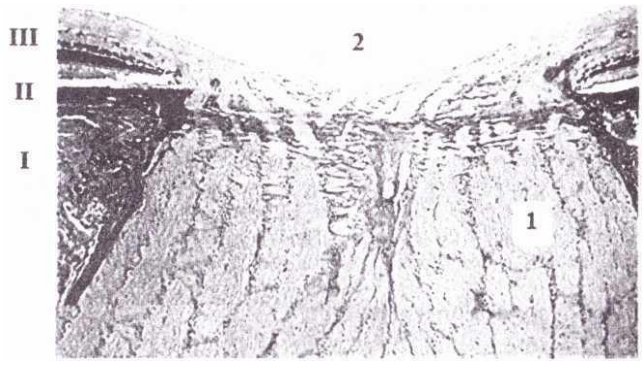


Figure 24. Optic disc. I - sclera, II - choroid, III- retina, 1 - layer of afferent fibers, 2 - optic disc

Functional systems of the eye

1. Refracting (dioptric) (the cornea, the aqueous humor, the lens, and the vitreous body) provides refraction light rays and a projection of observable subjects to the retina.

2. Accommodative (the iris, the ciliaty body, the lens) provides focusing the image on the retina by change of the form of the lens, regulates the intensity of lighting of the retina (owing to change of diameter of the pupil of iris).

3. Receptive (retina) provides perception and processing of light signals. Retinal histophysiology The conversion of the energy of light into nerve impulses is called phototransduction and involves two basic steps:

Step 1 is photochemical reaction that occurs in the outer segments of the rod and cone receptors. Photopigment contained in the disk membranes of the outer segment of rods and cones absorbs light energy (photons) and undergoes a biochemical changes. The visual pigment decomposes under influence of light. Visual pigment is a complex of two molecules: opsin and the chromophore. Opsin is a protein; the chromophore is the part affected by light - called retinal (a derivative of retinol, i.e., vitamin A). Absorbed light energy causes biochemical conformational changes in the chromophores.

Step 2 is changes in concentration of internal transmitters within the cytoplasm of the inner segment of the photoreceptors. These changes cause Na' channels (which are open in the resting state) to close. Closing Na + channels hyperpolarises the neuron. The hyperpolarisation of the outer segment spreads to the inner segment. Then the electrical signal is transmitted to the bipolar and then to the ganglion cells. The ganglion cells generate action potentials along their axons to the brain.

Accessory structures of the eye

1) Eyelids (fig.25) are mobile folds of tissue that protect the eyes. Each eyelid consists of a dense fibro-elastic plate, the tarsus, covered externally by thin skin and on the internal aspect by conjunctiva. Skeletal muscle of orbicularis oculi lies superficial to the tarsal plate. Within the tarsal plate lie some 12-30 sebaceous tarsal (Meibomian) glands. Associated with the eyelashes are sebaceous glands of Zeis and modified apocrine sweat glands of Moll.

2) lachrymal apparatus consists of the lacrimal glands, canaliculi, lacrimal sac, and nasolacrimal duct. Lachrymal glands are compound tubulo-alveolar. Alveoli are lined by cuboidal serous cells with basal myoepithelial cells. Canaliculi are lined by stratified squamous epithelium. Lachrymal sac and nasolacrymal duct are lined by pseudostratified epithelium.

3) Conjunctiva covers the anterior portion of the eye up to the cornea and the internal surface of the eyelids. It has stratified columnar with numerous goblet cells epithelium, its lamina propria consists of loose connective tissue.

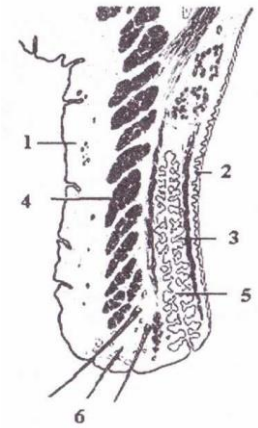


Figure 25. Eyelids. 1 - skin, 2 - conjunctiva, 3 — tarsal plate. 4 — orbicularis muscle, 5 — Meibomian glands, 6 - eyelashes

Development of the eye (fig. 26) The eye develops from 1) ectoderm forms the lens pit, which becomes deeper to form lens vesicle. Lens is formed from lens vesicle. Cornea is formed from ectoderm is over the lens vesicle.

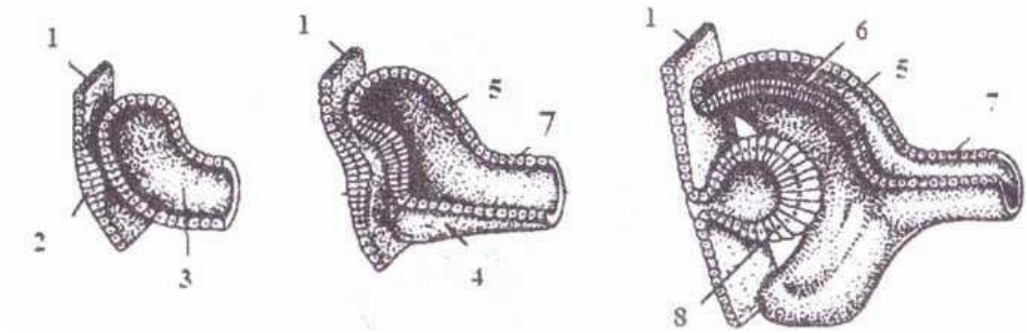


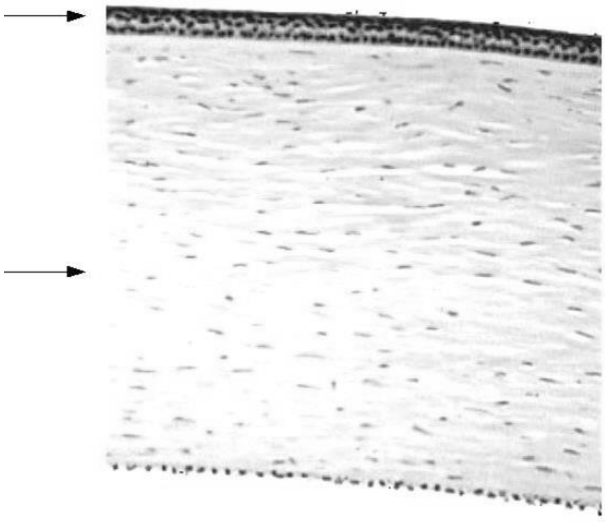
Figure 26. Development of eye. 1 - ectoderm (cornea), 2 — lens pit, 3 — optic vesicle, 4 - optic goblet, 5 - puter wall of the optic cup (layer of pigmented cells of the retina), 6 - inner wall of the optic cup (neurons of the retina), 7 - nerve stalk (optic nerve), 8 - lens vesicle (lens)

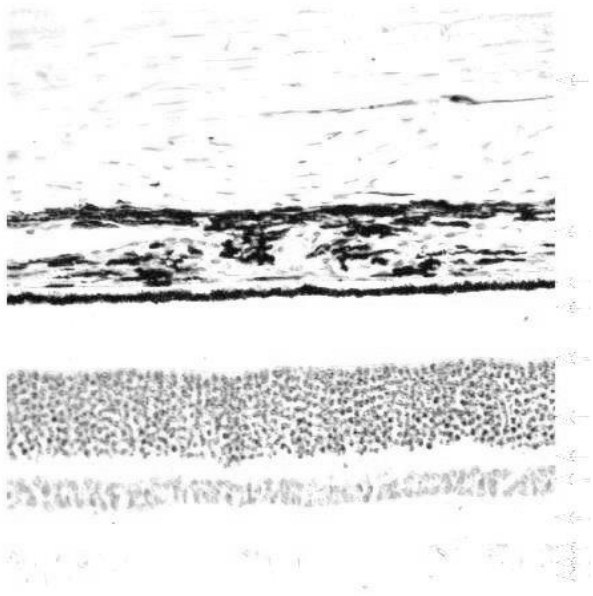
1).neuroectoderm forms optic vesicle, which differentiates to form optic cup. Outer wall of the optic cup forms the layer of pigmented cells of the retina. Inner wall of the optic cup forms the neurons of the retina. Nerve stalk forms optic nerve.
2) mesechyma forms the other components of the eye.

Practical lessons

1. Analyzers and their principle portions. Sense organs (classification due to the origin and structure of the receptor cells).
2. Visual organ. Eyeball: general structure, tunics, their portions and derivatives.
3. Fibrous and vascular tunics of eyeball, their portions, structure and functions. Cornea: microscopic and histochemical characteristic.
4. Inner eye tunic. Retina: nerve cells compounds. Ultrastructural and cytochemical characteristic of the photoreceptive cells.
5. Eye: dioptric and accomodative apparatus.

Paint and mark basic histological structure





Signature of teacher_____

SENSORY SYSTEM II. HEARING: THE AUDIORECEPTOR SYSTEM. TASTE & SMELL: THE CHEMORECEPTOR SYSTEM

Ear The ear consists of 3 parts:
1) external ear, which is responsible for reception of sound waves;
2) middle ear, transmitting sound waves in vibrations of fluid (perilymph) in a cochlea;
3) internal ear in which vibrations of a perilymph are transformed to nervous impulses.

External ear The external ear consists of:

- auricle (pinna), external auditory meatus,
- tympanic membrane. Auricle is composed of elastic cartilage covered by skin.

External auditory meatus. The wall of the outer third of the canal is formed by cartilage; the inner two-thirds of the canal lie in the petrous part of the temporal bone. The canal is lined by hairy skin containing sebaceous glands and modified apocrine sweat glands which secrete a waxy material called cerumen.

Tympanic membrane separates external ear from the middle, is composed of 3 layers:

- outer surface lined by skin;
- middle fibrous layer consisting of collagen fibers,

- inner mucous layer, lined by simple squamous epithelium.

Sound waves impinging on the tympanic membrane are converted into mechanical vibrations which are then amplified by auditory bones.

Middle ear The middle ear consists of:

tympanic cavity,

auditory ossicles,

auditory tube.

Tympanic cavity is irregular space in the temporal bone lined by simple squamous epithelium. In the medial wall of the tympanic cavity are 2 membrane-covered regions: the oval and the round windows. Auditory ossicles (the malleus, incus, and stapes) transmit the mechanical vibrations generated in the tympanic membrane to the inner ear. These bones are articulated by synovial joints and covered by simple squamous epithelium. Auditory tube communicates the tympany cavity with the nasopharynx and permits equalization of pressure changes with the external environment.

Internal ear. The internal ear consists of a fluid-filled membranous labyrinth lying within a labyrinth of spaces in the temporal bone (the bone labyrinth). The membranous labyrinth is bound down to the walls of the bone labyrinth by thin strands of connective tissue in various places but in the main is separated from the bony walls by a fluid-filled space. The fluid within the membranous labyrinth is known as endolymph and the fluid in the surrounding perimembranous space is known as perilymph. The bone labyrinth may be divided into 3 main areas (fig.27): 1) vestibule, housing the saccule and the utricle; 2) behind this, three semicircular canals enclose the semicircular duct; 3) the anterolateral cochlea contains the cochlear duct.

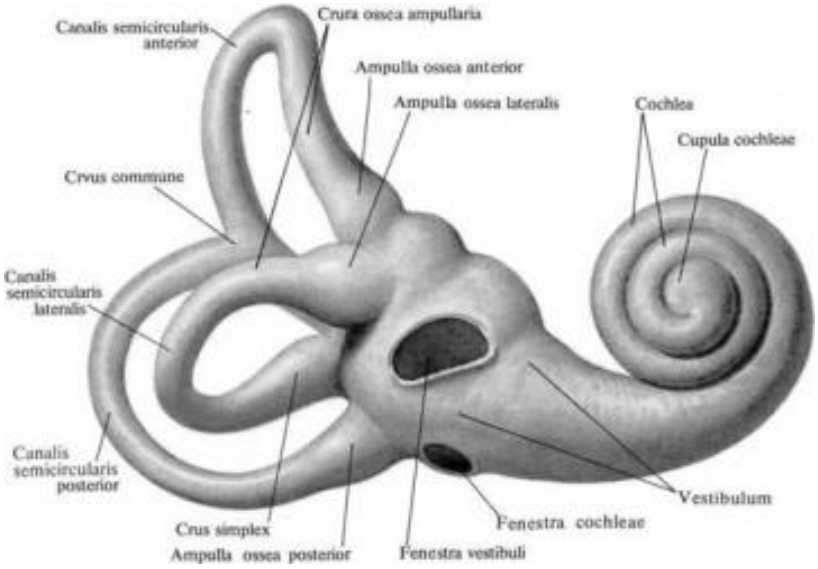


Figure 27. The osseous labyrinth. 1 - cochlea, 2 - saccule, 3 — utricle, 4,— semicircular canals, 5 - ampullae, 6 - tubular ducts containing endolymp

The cochlea, about 35 mm in length, makes two-and-one -half turns around a bony core - the modiolus (fig. 28). Receptor organs of the saccule and utricle. The saccule and utricle are two dilated regions of the membranous labyrinth lying

within the vestibule of the inner ear. The saccule and utricle are lined by simple cuboidal epithelium but in each there is a region of highly specialised epithelium called the macula of the saccule and nmcula of the utricle.

The maculae are made up of two basic cell types, sensory (receptor) cells and supporting cells (fig. 29). 1. The supporting cells are tall and columnar with basally-located nuclei and microvilli at their free surface. 2. The sensory cells (hair cells) lie between the support cells.

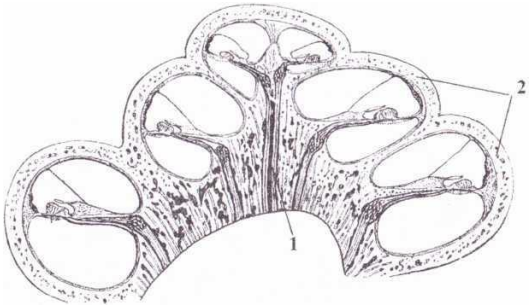


Figure 28. Schematic diagram of a cochlea. 1 - turns of cochlea, 2 – modiolus

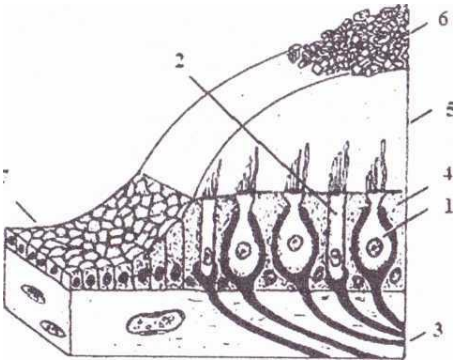


Figure 29. The structure of maculae. 1 - receptor type I hair cell, 2 - receptor type II hair cell, 3 - nerve endings, 4 - supporting cell, 5 - gelatinous layer (the otolithic membrane), 6 — otoliths, 7 — epithelium of membranous labyrinth

Each sensory (receptor) cell has a single large eccentrically- located kinocilium, which is immotile and number of stereocilia (microvilli) projecting from its surface (fig. 30).

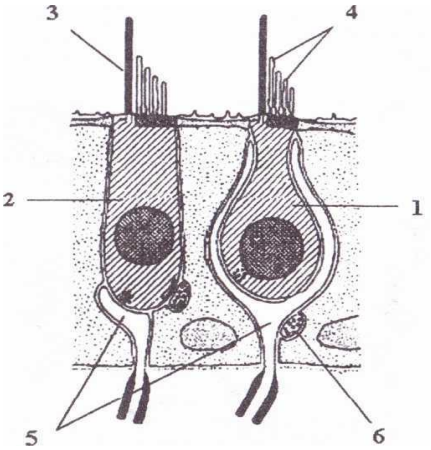


Figure 30. Sensory (receptor) hair cells. 1 - type I hair cell, 2 - type II hair cell, 3 - kinocilium, 4 - stereocilia, 5 - afferent nerve endings, 6 - efferent nerve endings

Type II hair cells have columnar shape. They have only small afferent nerve endings at their bases. Both types have efferent nerve endings that are inhibitory. Covering this epithelium is a thick, gelatinous glycoprotein layer (the otolithic membrane). At the surface of this membrane there is a mass of crystals mainly composed of calcium carbonate (otoliths) (fig.31).

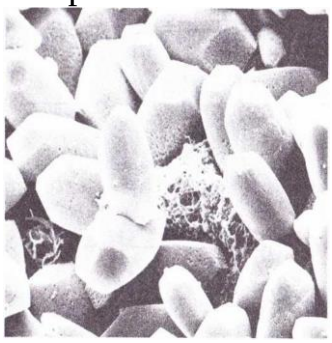


Figure 31. Scanning electron micrograph of the surface of the macula showing the otoliths.

Function of the maculae.The function of the maculae is to the maintenance of balance by providing sensory information about the static position of the head in space. This is of particular importance when the eyes are closed, or in the dark or under water. When the head is moved from a position of equilibrium, the otolithic membrane tends to move w'ith respect to the receptor cells, thus bending their stereocilia. When the stereocilia are bent in the direction of the cilium, the receptor cell undergoes excitation and, when the relative movement is in the opposite direction, excitation is inhibited. Receptor cells of the semicircular canals Three semicircular canals arise from the vestibule of the inner ear, each containing a membranous semicircular duct which opens at both ends into the utricle. At one end of each duct there is a dilated portion, the ampulla, which contains a receptor organ, called the crista ampullaris (fig. 35).

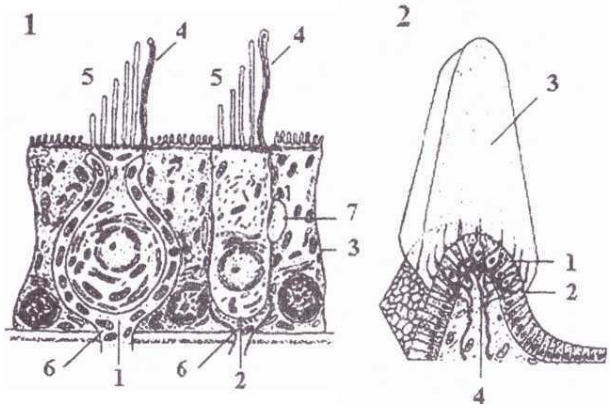


Figure 32 - 1. Infrastructure of sensory cells of crista ampullaris: 1 - type I hair cell, 2 - type II hair cell, 3 - supporting cell, 4 - kinocilium, 5 — stereocilia, 6 - - afferent nerve endings, 7 - efferent nerve endings **Figure 32 - 2.** Crista antpuliaris: 1 - receptor hair cell, 2 - supporting cell, 3 - cupula, 4 - nerve endings.

Each crista ampullaris is an epithelial structure situated on a ridge of supporting tissue. The receptor cells are of two morphological types, one are flask-shaped and the other are more slender (columnar). The receptor cells are supported by a single layer of columnar cells which is continuous with the simple cuboidal epithelium lining the rest of the membranous labyrinth. Like those of the maculae, the receptor cells of the cristae have numerous stereocilia and a single cilium. The stereocilia and the cilia of the sensory receptors are embedded in a gelatinous glycoprotein layer; it is a conical shape called a cupula. The cupula does not contain otolithic crystals.

Function of the crista ampullaris. The crista ampullaris accept angle accelerations. When the head is moved in the plane of a particular semicircular canal, the inertia of the endolymph acts so as to deflect the cupula in the opposite direction. The stereocilia of the sensory cells are then deflected towards or away from the cilia, resulting in excitation or inhibition respectively.

Cochlear duct. When observed in histological sections, the cochlea appears to be divided into 3 spaces (fig. 36): scala vestibule (above), scala media (cochlear duct) in the middle, scala tympani (below). The cochlear duct, which contains endolymph, ends blindly at the apex of the cochlea. Other two scalae contain perilymph and are one long tube, beginning at the oval window and terminating at the round window. They communicate at the apex of the cochlea via an opening known as the helicotrema.

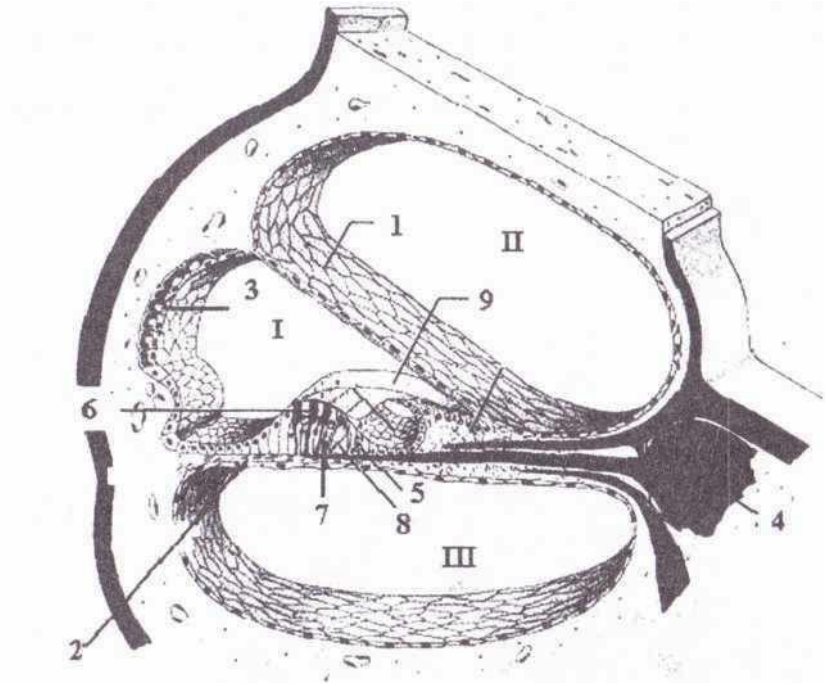


Figure 33. Schematic diagram of the cochlea. I - scala media, II - scala vestibule, III - scala tympani; 1 - vestibular membrane, 2 - basilar membrane, 3 - stria vascularis, 4 - spiral ganglion, 5 - inner hair cells, 6 - outer hair cells, 7 - pillar cells, 8 - inner tunnel, 9 - tectorial membrane

Histological structure of the cochlear duct

1).Vestibular (Reissner's) membrane consists of two layers of squamous epithelium, one derived from the scala media and the other from the lining of the scala vestibuli.

2).Stria vascularis is a vascularised epithelium located in the lateral wall of the cochlear duct. It consists of three types of cells: marginal, intermediate, and basal. Marginal cells are responsible for the characteristic ionic composition of endolymph.

3) . Basilar membrane separates the scala media and scala tympany and supports special auditory receptors is called the spiral organ of Cord; it contains hair cells that respond to different sound frequencies. The basilar membrane is a thick layer of amorphous ground substance, containing fibrils. Spiral organ of Corti Organ of Corti consists of 2 types of cells (fig.37): 1) sensory (hair) cells, 2) supporting cells.

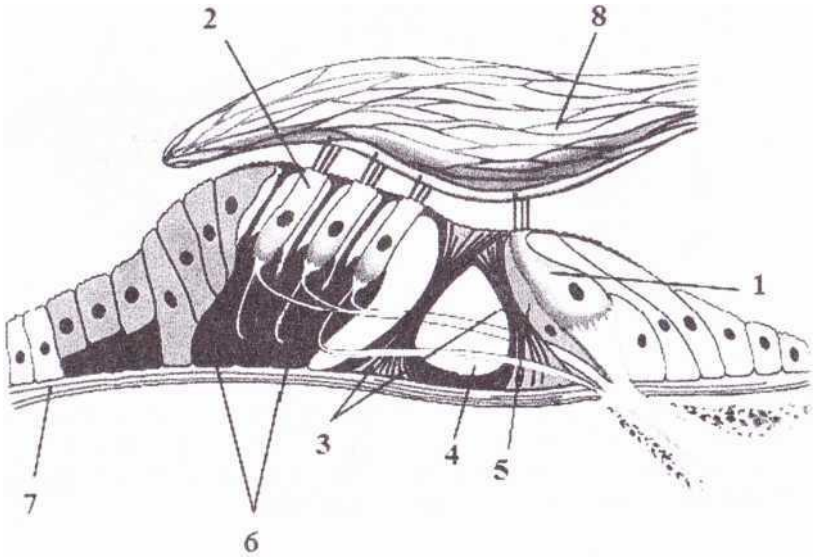


Figure 34. Schematic diagram of the spiral organ of Corti. 1 - inner hair cell, 2 - outer hair cells, 3 - pillar cells, 4 - tunnel of Corti, 5 - inner phalangeal cells, 6 - outer phalangeal cells, 7 - basilar membrane, 8 - tectorial membrane.

At the centre of the organ is a triangular-shaped canal, the inner tunnel or tunnel of Corti. It is bounded on each side by a single row of tall columnar cells called pillar cells. On the inner aspect of the inner row of pillar cells is a single row of flaskshaped cells called inner phalangeal cells which support a single row of inner sensory (hair) cells.

Beyond the outer row of pillar cells there are three to five rows of outer phalangeal cells which support the same number of rows of outer sensory (hair) cells. Both types of hair cells are columnar. The most characteristic feature of these cells is the V-shaped (outer hair cells) or liner (inner hair cells) (fig.38) array of stereocilia. The tips of the stereocilia of the sensory cells are embedded in the gelatinous glycoprotein tectorial membrane.

Function of the organ of Corti. Sound waves produce vibrations of a tympanic membrane. These vibratioas are transmitted to the auditory' ossicles transferring them on a perilymph and a basilar membrane. The basilar membrane is thinnest at the base of the cochlear and thickest at the apex. It appears that, at every point on

the spiral, the membrane is ’t uned1 to vibrate to a particular frequency of sound waves reaching the ear. The process of transduction of mechanical energy into electrochemical energy' probably results from deformation of the stereocilia of the sensory' cells. An electric potential is transferred to the terminals of dendrites of bipolar cells of a spiral ganglion (their axons form a cochlear nerve). More than 90 % of afferent nerve fibrils approach to inner hair cells and to more numerous outer hair cells - only 10 %.

Development of the membranous labyrinth of the ear. The membranous labyrinth is derived from a area of surface ectoderm overlying the developing rhombencephalon (hindbrain) (fig. 39). This area is called the optic placode.

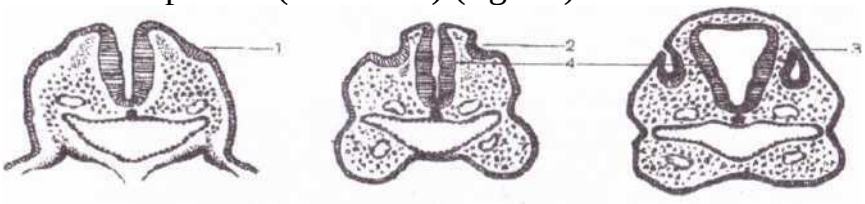


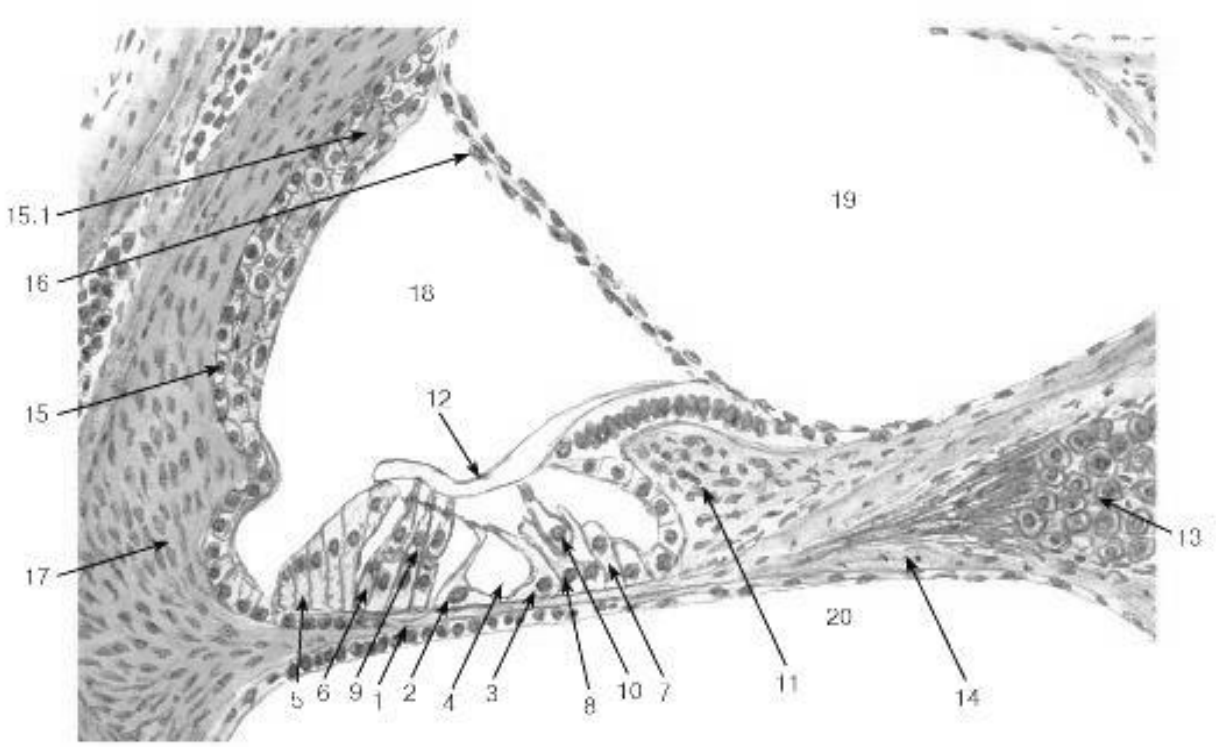
Figure 35. Development of the ear. 1 — otic placode, 2 - otic pit, 3 — 3 - otic vesicle, 4 – hindbrain.

The otic placode becomes depressed to form the otic pit. The pit then becomes rounded to form the otic vesicle, which separates from the surface ectoderm. The otic vesicle is at first an oval structure. By differential growth of various parts of its wall, it gives rise to the comprising the membranous labyrinth. Localized areas of the epithelium of the membranous labyrinth undergo differentiation to form specialized sensory end organs of hearing, and of equilibrium.

Practical lessons

1. Audiovestibular organ. Cochlear membranous labyrinth (structure and functions). Corti’s organ: histophysiology.
2. Vestibular organ. Vestibular portion of the membranous labyrinth: disposition, structure and functions of the utricle and saccule macules and ampullary crests.

Paint and mark basic histological structure



Signature of teacher_____

Taste. Taste is a sensation perceived by taste buds, receptors located principally on the tongue and in smaller numbers on the soft palate and laryngeal surface of the epiglottis. Lingual taste buds are embedded within the stratified epithelium of the circumvallate, foliate, and fungiform papillae (fig.40)

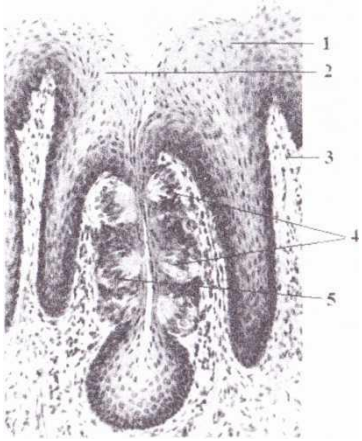


Figure 35. Papillae of the tongue. 1 - papilla, 2 - stratified epithelium, 3 — connective tissue, 4 - taste bud, 5 - gustatory cells of the taste bud.

I here are about 3000 taste buds on the tongue of an adult person. There are four main tastes - sweet, salty, sour and bitter. These four main tastes are felt by different portion of the tongue. The tip of our tongue senses salt and sweet. The

taste buds at the sides detect sour taste. The rear portion of the tongue detects bitter taste. The taste bud is a ban-el-shaped organ extending the full thickness of the epithelium and opening at the surface via taste pore (fig. 36). Each taste bud contains 20-30 long spindle-shaped cells. 3 types of cells are described in the taste bud: **gustatory cells, supporting cells, basal cells.**

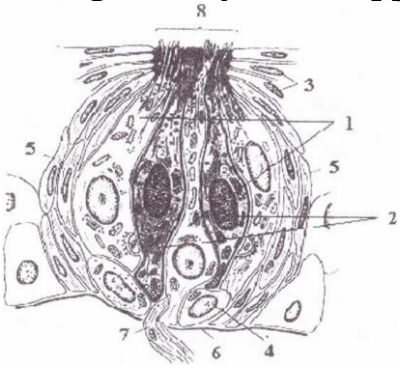


Figure 36. Structure of a taste bud. 1 - supporting cells, 2 - gustatory cells, 3 - epithelial cells of the tongue, 4 - basal cells, 5 — peripheral cells, 6 - basal membrane, 7 - nerve fibers, 8 - taste pore

Gustatory cells are fusiform cells and lie in the center of the bud. Supporting cells are crescent shaped and surround the gustatory cells. Both gustatory and supporting cells have long microvilli extending into the taste pore. Basal cells are precursors of one or both of the other cell types. **ESI Smell**: the chemoreceptor system The olfactory chemoreceptors are located in the olfactory epithelium in the nasal cavity. This is a pseudostratified columnar epithelium composed of 3 types of cells (fig. 42); **supporting cells, basal cells. olfactory cells.**

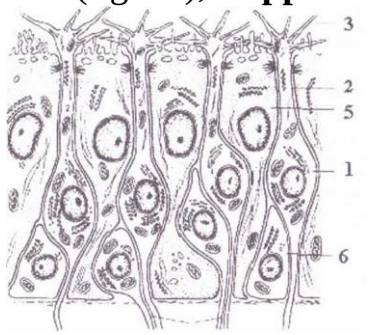


Figure 37. Olfactory epithelium. 1 - olfactory cells, 2 — dendrites, 3 — olfactory cilia, 4 - axons, 5 - supporting cells, 6 - basal cells.

The supporting cells have broad apexes and narrow bases. Their surface has microvilli. The cytoplasm contains yellow pigment that is responsible for the colour of the olfactory mucosa. The basal cells are small, spherical or cone-shaped. Basal cells are precursors of both olfactory and supporting cells. The olfactory cells are the bipolar neurons. Their apexes possess dilated areas from which arise 6-20 cilia. These cilia are long and immotile and are the structures that respond to odoriferous substances by generating a receptor potential. The axons of olfactory cells unite in small bundles directed toward the central nervous system.

INTEGUMENTARY SYSTEM

Overview of the integumentary system The integumentary system comprises of the skin and its derivatives: hair, nails, sweat glands, sebaceous glands, mammary glands. The skin is the largest organ of the body, constituting 15-20% of total body mass and, in adults, forming 1,2 - 2,3 m2 of body surface.

Functions of the skin

1. Protection (mechanical, UV radiation, water conservation) and immune response (the skin is the first line of defence against pathogens and toxins in the environment).
2. Sensation Skin is sensitive and causes the body to react to heat, cold, sharp pain, and pressure. Skin can provide protection from injury.
3. Body temperature regulation Skin controls body temperature by contracting or expanding the blood vessels in the skin. Dilated blood vessels release heat from the body. Contracted blood vessels restrict heat loss. Increased perspiration cools the body while decreased perspiration keeps the body warmer,
4. Storage and nutrient synthesis Skin stores water, lipids, cholesterol and vitamins A, D, E and K. Interaction with UV light synthesis vitamin D.
5. Excretion The skin excretes urea and excess minerals.
7. Absorption The skin absorbs oxygen, carbon dioxide and nitrogen in small amounts. It also absorbs many of the chemicals that are in the environment such as pollution and chemicals from body care and cleaning products.

Organization of the skin. The skin is composed of the epidermis and the dermis The junction of dermis and epidermis is irregular, and projections of the dermis called papillae. Beneath the dermis lies the hypodermis. or subcutaneous tissue (fig.38).

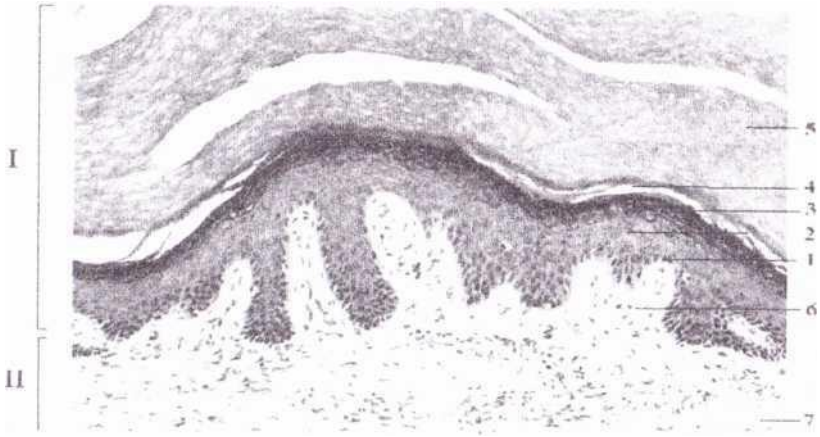


Figure 38. Photomicrograph of human thick skin. I - epidermis: 1 - stratum basale, 2 — stratum spinosum, 3 — stratum granulosum, 4— stratum lucidum, 5 - stratum comeum; II - dermis: 6 - papillary layer, 7 - reticular layer/

Epidermis The epidermis consists of stratified squamous keratinised epithelium and has **5 layers**:

1. **Stratum basale** consists of a single layer of basophilic columnar cells (keratinocytes) resting on the basal lamina at the dermal-epidermal junction.
2. **Stratum spinosum** consists of polygonal cells joined to one another by cytoplasm processes. Mitosis occurs in both the above layers and such two layers together are called stratum germinativum.
3. **Stratum granulosum** consists of I or 5 layers of flattened polygonal cells. These cells contain **kerotohyalin** granules.
4. **Stratum lucidum** is thin layer of flattened eosinophilic cells. The cells are dying or already' dead and contain droplets of **eleidin**, precursor of keratin.
5. Stratum corneum consists of 15-20 layers of flattened **anucleate** keratinized cells whose cytoplasm is filled with scleroprotein, **keratin**. The most superficial cells are continuously lost and are replaced by proliferation of cells that arise from mitotic activity in stratum germinativum.

Regional differences if the skin The epidermis of palm and sole are thick, has 5 layers, is hairless. Elsewhere, the skin possesses a much thinner epidermis ands is called thin It contains hair follicles. Its epidermis contains stratum basale, stratum spinosum, stratum granulosum, and a thin stratum comeum. Stratum lucidum is absent. Cells of the epidermis The cells of the epidermis consist of different types: keratinocytes and nonkeratinocytes. Keratinocytes are the predominant cell type of the epidermis. These cells originate in the basal epidermal layer. Their main functions are:

- production of the major structural protein of the epidermis, keratin;
- formation of the epidermal water barrier. Nonkeratinocytes
- 1. Melanocytes are pigment-producing cells. These cells are derived from neural crest and produce melanin, a dark brown pigment. The bodies of these cells are situated at the stratum basale, and highly branching processes are situated at the stratum spinosum (fig. 39).

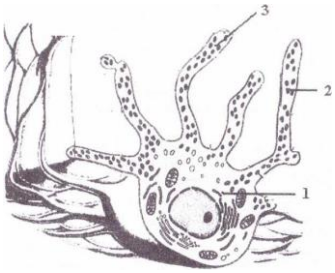


Figure 39. Schematic diagram of melanocyte. 1 - cell body, 2 - processes, 3 - melanin granules.

2. **Langerhans' cells** are star-shaped cells, found mainly in the stratum spinosum of the epidermis. They are bone-marrow-derived macrophages that are capable of binding, processing, and presenting antigens to T lymphocytes. These cells have a significant role in immunologic skin reactions.

3. **Merkel's cells** generally present in the thick skin of palms and soles. Free nerve ending are present at the base of Merkel's cells. These cells may serve as sensory mechanoreceptors.

Dermis.The dermis is a connective tissue layer containing blood and lymphatic vessels, and nerves of the skin. It also contains hair follicles, sweat and sebaceous glands **The dermis contains 2 layers -** the **superficial papillary layer and the deeper reticular layer**. The thin papillary layer is composed of loose connective tissue; delicate collagen network contains predominately type 1 and type 111 collagen molecules; elastic fibers form an irregular network. Sections of skin cut perpendicular to the surface reveal numerous finger-like connective tissue protrusions, dermal papillae that project into the undersurface of the epidermis. Epidermal ridges are epidermal protrusions that project into the dermis. The ridges and papillae are most prominent in the thick skin of the palmar and plantar surfaces. Ridges form a distinctive pattern that is genetically unique to each individual. These patterns are the basis of the science of dermatoglyphics, or fingerprint or footprint identification. The reticular layer is thicker, composed of irregular dense connective tissue. This layer contains thick, irregular bundles of mostly type I collagen and coarser elastic fibers. This elastic network is responsible for the elasticity of the skin. The collagen and elastic fibers form regular lines of tension in the skin, called Langer's lines. Skin incisions made parallel to Langer's lines.

Hypodermis (subcutaneous tissue) The hypodermis consists of loose connective tissue that binds the skin to the subjacent organs, making it possible for skin to slide over them. The hypodermis contains fat cells that vary in number according to the area of the body, and in size according to the nutritional status of the individual. Sources of development of the structural components of the skin Epidermis derived from the skin ectoderm. Dermis derived from dermatomes of the somites of the paraxial mesoderm.

Hypodermis derived from mesenchyme.

Derivatives of the skin.

Hairs. The hairs are elongated keratinized structures. Their colour, size, and disposition vary according to race, age, sex, and region of the body. The hair consists of 2 parts:

- shaft projects above the skin;
- root is embedded within the skin epidermal invagination termed the hair follicle. The hair follicle is located in the dermis (fig.40).

The dermal papilla is at the base of the hair follicle. The dermal papilla contains a capillary network. The sebaceous gland is situated in the upper follicle, as is the erector muscle of the hair. **The hair follicle consists of:**

- hair bulb,
- inner root sheath,
- hair shaft.

New hair is made inside the onion-shaped hair bulb that lies within the hair follicle. It has a cavity in which the dermal papilla is embedded. Special cells in the hair bulb produce the pigment that colours hair. The pigment is called melanin.

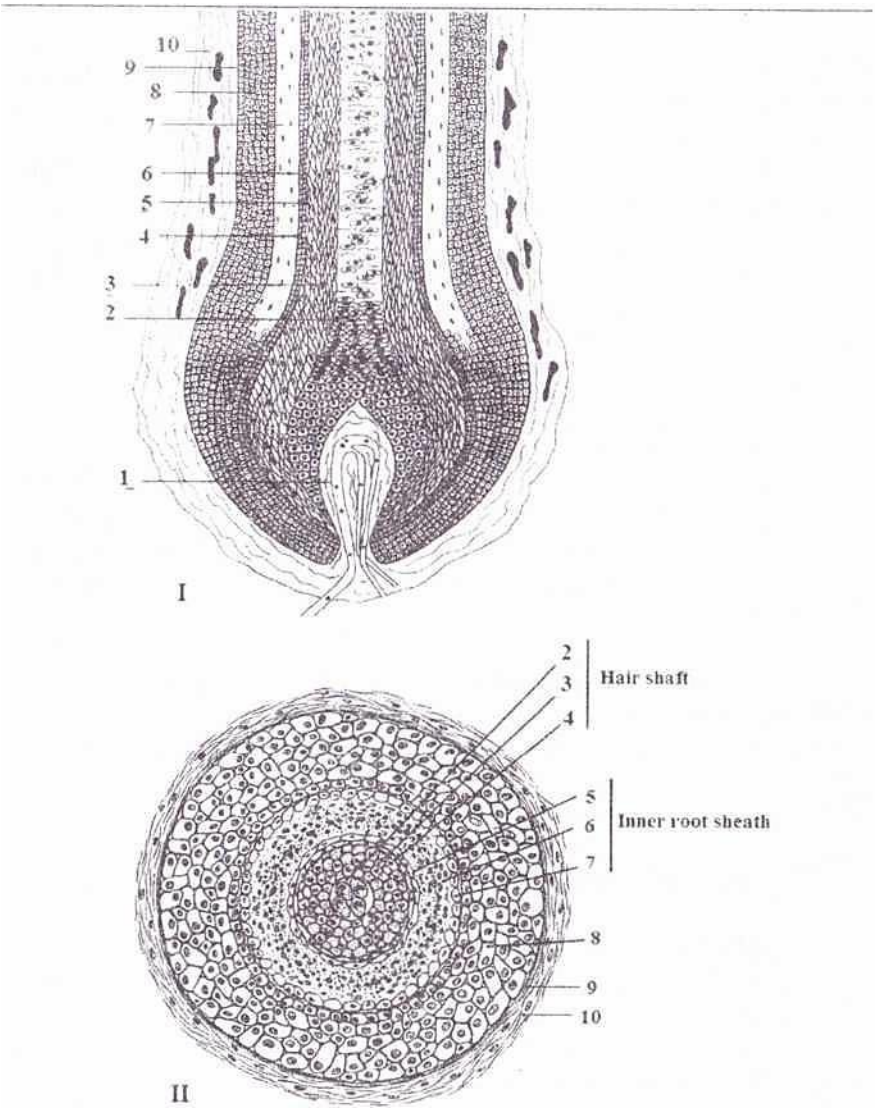


Figure 40. Schematic diagram of the hair follicle and hair. I - longitudinal section, II - cross section; 1 - papilla, 2 - medulla, 3 - cortex. 4 - hair cuticle, 5 - inner root sheath cuticle, 6 - Huxley's layer, 7 - Henle's layer, 8 - external root sheath, 9 — glassy membrane, 10 - dermal connective tissue

The **bulb contains the hair matrix, the germ layer that forms the inner root sheath, and the hair shaft that is composed of three layers**:

- medulla,
- cortex and
- hair cuticle.

Medulla is the innermost layer. The middle layer - cortex - contains fibers which are important for hair's strength and elasticity. The outermost layer is known as the hair cuticle. The cuticle is thin and colourless and serves to protect the cortex. Inner root sheath is derived from the stratum corneum of the epidermis and is composed of three layers:

- internal root sheath cuticle (keratinized cells),
- granular epithelial (Huxley's) layer (1-3 layers of homy, flattened, nucleated cells rich in trichohyalin granules) and

- pale epithelial (Henle's) layer (a single layer of cuboidal epithelium forming the outer boundary of the inner stratum of a hair follicle).

Outer root sheath surrounds the hair follicle and secures the hair shaft within the follicle. Outer root sheath is derived from the stratum germinativum of the epidermis and is composed of several layers of cells similar to the epidermis. External to this layer is a homogeneous glassy membrane corresponding to the basal lamina of the epidermis. Entire root sheath (inner and outer) is enclosed by connective tissue sheath derived from the dermis.

Nails The nail is plate of keratinised epithelial cells on the dorsal surface of each distal phalanx (fig.41).

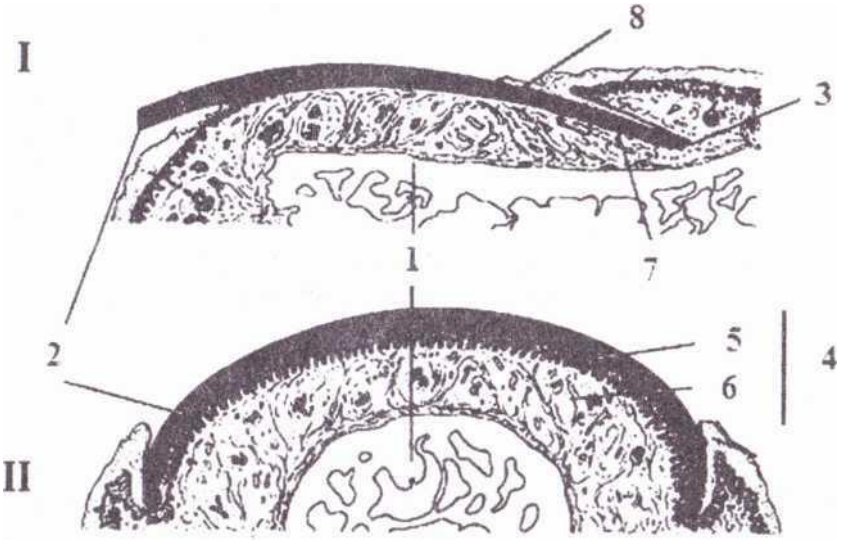


Figure 41. Nail and its components. I — longitudinal section, II — cross section; 1 - distal phalanx, 2 - nail plate, 3 - nail root. 4 - nail bed: 5 - epithelium, 6 - connective tissue, 7 - nail matrix, 8 – eponychium

The proximal part of the nail is the nail root. The epithelium covering the nail root consists of usual layers of cells. The stratum corneum of this epithelium forms the eponychium, or cuticle. The nail plate rests on the bed of epithelium called nail bed. Only the stratum basale and stratum spinosum of epidermis and connective tissue are present in the nail bed. The part of the nail bed supporting the root ol the nail is called nail matrix, from which new formation of nail takes place.

Glands of the skin

Sweat glands. The sweat glands produce sweat or perspiration. Besides excretion these glands help in temperature regulation by sweating. There are 2 types of sweat glands - merocrine and apocrine. The merocrine sweat glands are present in the skin of all parts of the body. They are simple, coiled tubular glands whose ducts open at the skin surface. The swear gland consists of 2 parts (fig.42):

Figure 42. Sweat gland. 1 - secretory portion, 2 - secretory cells, 3 - myoepithelial cells, 4 –duct.

- **secretory portion** lies deep in the dermis, lined by a single cuboidal epithelium. Myoepithelial cells surround secretory cells;
- **ducts are** lined by 2 layers of dark cuboidal cells.

The apocrine sweat glands are present in the subcutaneous tissue ol the axillary, areolar, and anal regions. Their ducts open into hair follicles. These glands become fully developed only after puberty. They are large and branched tubular glands. The lumen of secretory part is large. The lining of epithelium may be squamous, cuboidal or columnar. The secretions of apocrine sweat glands are viscous.

Sebaceous glands

The sebaceous glands are branched alveolar glands of the holocrine type. The secretory portion of the gland (the acini) consists of 2 types of epithelial cells (fig. 43):

- small outmost basal cells rest on the basal lamina.
- inner cells are larger, more rounded and filled with lipid. The ducts usually end in the upper portion of the hair follicle.

They are very short and lined by stratified epithelium. The secretion of the sebaceous glands is called sebum. Its oily nature helps to keep the skin and hair soft. It helps to prevent dryness of the skin and also makes it resistant to moisture.

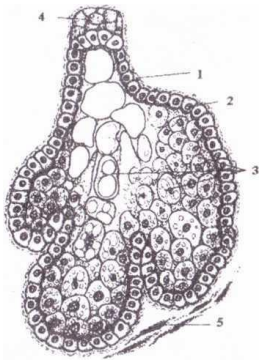
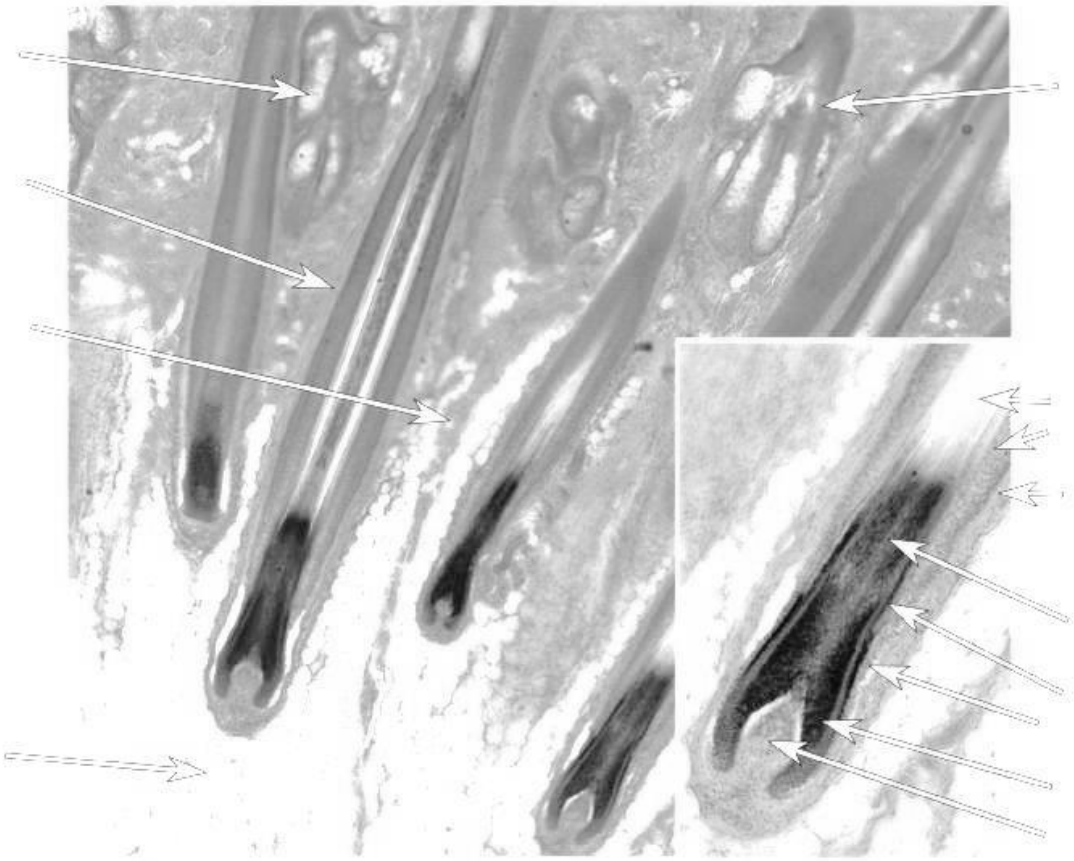


Figure 43. Sebaceous gland. 1 - basal lamina, 2 - basal cells, 3 - inner cells, 4 - duct, 5 - arrector pili

Practical lessons

1. Structure and functions of the skin. Physiologic regeneration of epidermis
2. Structure and functions of the hair.
3. Structure and functions of the nail and its components.
4. Structure and functions of the sebaceous gland.
5. Structure and functions of the sweat gland.

Paint and mark basic histological structure



Signature of teacher_____

CARDIOVASCULAR SYSTEM

Overview of the cardiovascular system The cardiovascular system consists of the blood and lymphatic vascular systems. The blood vascular system is composed of the following structures:

- the heart, whose function is to pump the blood,
- the arteries, whose function is to carry the blood with nutrients and oxygen to the tissues,
- the capillaries, a diffuse network of thin tubules through whose walls the interchange between blood and tissues takes place,

- the veins, whose function is to convey products of metabolism toward the heart.

The lymphatic vascular system begins in the lymphatic capillaries, blind-ended tubules that terminate in the blood vascular system emptying into the large veins near the heart. The function of the lymphatic system is to return to the blood the fluid of the tissue spaces.

General structure of blood vessels.The blood vessels have a common basic structure. Blood vessels are usually composed of the following layers, or tunics (fig. 44).

I.tunica intima consists of:

1) layer of endothelial cells lining the vessels interior surface; these cells rest on a basal lamina;

2) subendothelial layer, consisting of loose connective tissue;

3) in arteries the intima is separated from the media by an internal elastic lamina, composed of elastin;

II. **tunica media** consists of smooth muscle cells; interposed among the smooth muscle cells are variable amounts of elastic and reticular fibers. In larger arteries, a thinner external elastic lamina separates the media from the outer tunica adventitia;

III. tunica adventitia consists of loose connective tissue with longitudinally oriented collagen and elastic fibers; it contains nerves and vasa vasorum.

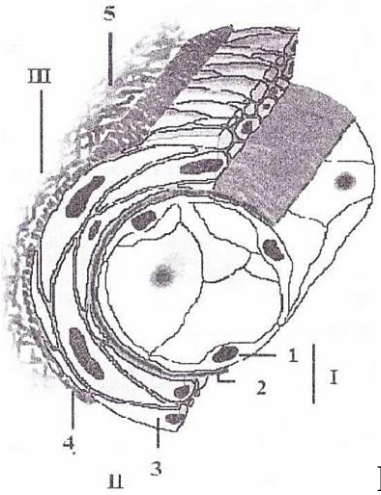


Figure 44. Schematic diagram of blood vessel wall. I-tunica intima: 1 — endothelial cells, 2 - internal clastic lamina, II - tunica media: 3 - smooth muscle cells, 4 - external elastic lamina, III - tunica adventitia: 5 - loose connective tissue

Blood vessels are structurally adapted according to hemodynamic factors. 0

Arteries. Arteries transport blood to tissues. They resist changes in blood pressure in their initial portions and regulate blood flow in their terminal portions. There are **3 main types of arteries:**

- **Elastic (large) arteries**
- **Elastic - muscular (medium) arteries**
- **Muscular (small arteries)**

Elastic arteries. The blood is pumped from the heart into large, elastic (conduction) arteries. The aorta and its large branches are the typical elastic arteries. **Elastic arteries have the following characteristic** (fig.50):

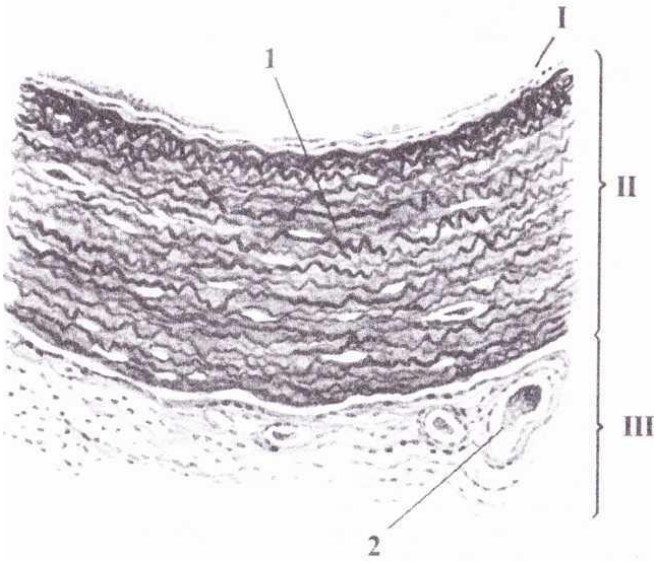


Figure 45. Schematic diagram of the aorta. I - tunica intima, II - tunica media, 111 — tunica adventitia, 1 - perforated elastic laminae, 2 - vasa vasorum

Elastic arteries.

The aorta and its large branches are the typical elastic arteries.

I.tunica intima:

1) endothelium is simple squamous epithelium, located on the **basement membrane,** is smooth without of folds;

2) subendothelial layer is thick, consists of loose connective tissue and includes a plexus of elastic fibers, which is formed by two layers: ***the inner - elastic fibers are circular, the outer - elastic fibers are located longitudinally.***

II. tunica media consists of concentrically arranged 40-50 perforated elastic laminae and circular elastic fibers.

III. tunica adventitia consists of loose connective tissue, contains longitudinally elastic fibers, blood vessels and nerves.

Muscular – elastic arteries (a. subclavian)

I. tunica intima forms numerous small folds, and contains:

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer contains of loose connective tissue ,

3) ***internal elastic lamina*** is prominent and forms small wavy folds;

II. tunica media comprises a thick layer of circumferentially arranged 50:50 smooth muscle and elastic fibers;

external elastic lamina is present, forms small wavy folds ;

III.tunica adventitia consists of loose connective tissue, contains elastic and collagen fibers, blood vessels and nerves.

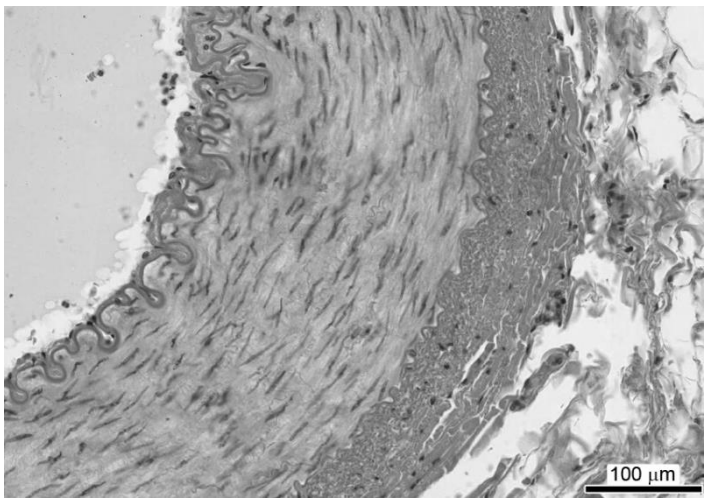


Figure 46 A. Photomicrograph of the muscular elastic artery. I — tunica intima, II - tunica media, III - tunica adventitia

Muscular arteries. Blood passes from the elastic arteries of intermediate type into the muscular (distribution) arteries. Most of the arteries in the human body are muscular arteries. In muscular arteries (fig.46.B): the blood passes at a reduced pressure and speed. The size of their lumen is controlled by contraction or relaxation of smooth muscle on their wall.

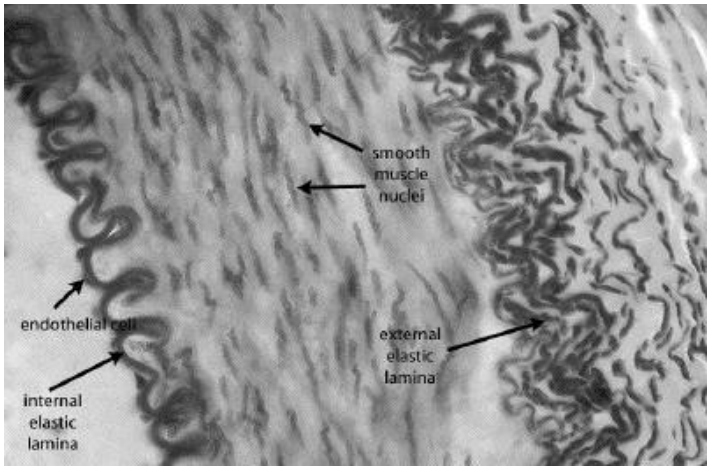


Figure 46B. Photomicrograph of the muscular artery. I — tunica intima, II - tunica media, III - tunica adventitia

Muscular arteries have the following characteristic

I. tunica intima forms numerous small folds, and contains:

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer contains of loose connective tissue,

3) ***internal elastic lamina*** is prominent and forms small wavy folds;

II. tunica media comprises a thick layer of circumferentially arranged smooth muscle;

external elastic lamina is present and forms small wavy folds;

III.tunica adventitia consists of loose connective tissue, contains elastic and collagen fibers, blood vessels and nerves.

Arterioles These are generally less than 0,5 mm in diameter and have relatively narrow lumens. The wall of the arterioles contains:

I. **tunica intima** forms numerous small folds, consists of:

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer is very thin , consists of loose connective tissue.

3) internal elastic lamina is prominent and forms small wavy folds;

II. tunica media composed **of one or two spirally arranged layers** of smooth muscle cells; external elastic lamina is absent;

III.tunica adventitia is thin consists of loose connective tissue**,** blood vessels and nerves.

Function of arterioles:

regulate the flow of blood to organs.

Specialized sensory structures in arteries participate in reflex regulation of a circulation.

*I.**The carotid sinus** is near the bifurcation of the common carotid artery , this is dilating of a lumen of an internal carotid artery immediately near of its ramification from the common carotid artery. There are numerous baroreceptors in the tunic adventitia of carotid sinus. From the baroreceptors information enters in the centers regulating activity of cardiovascular system.*

*II. **Carotid body** is small structure encountered near the bifurcation of the common carotid artery acts as chemoreceptors sensitive to low oxygen tension, high carbon dioxide concentration, and low arterial blood pH.*

The carotid body consists of glomus cells (type I cells) and sheath cells (type II cells) surrounded by a rich vascular supply whose capillaries are of the fenestrated type. Most of the nerves of the carotid body are afferent fibers.

III. Aortic bodies and jugular glomera are similar in structure to the carotid body and are thought to have a similar function.

Veins. The veins return blood to the heart, aided by the action of smooth muscle and specialized valves**. Classification of the veins:**

- **Unmuscular** (atypical)
- **Muscular**
  1) with weak development of muscular elements;
  2) with middle development of muscular elements;
  3) with strong development of muscular elements

Unmuscular veins The unmuscular veins are in organs with dense walls (meninges, bones, spleen, etc.) with which they strongly fuse external tunic. The wall of these veins **consists of endothelium**, located on the **basement membrane** which is **surrounded by layer of a connective tissue**. Smooth muscle cells are absent.

Muscular veins with weak development of muscular elements. The muscular veins with weak development of muscular elements (fig. 47) are above the level of the heart on which blood goes passively owing to weight.

The structure of the wall of these vessels has the following characteristics:

I. tunica intima:

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer is weak-developed formed loose connective tissue,

II. **tunica media** is thin with small amount **circumferentially** arranged of **smooth muscle cells;**

III**. tunica adventitia** contains loose connective tissue, blood vessels and nerves.

.

Muscular veins with middle development of muscular elements The muscular veins with middle development of muscular elements are on the level of the heart. **The structure of the wall of these vessels has the following characteristics**:

I. **tunica intima** forms the valves and consists of:

1) endothelium- is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer is weak-developed, formed loose connective tissue ,

II**. tunica media** consists of few layers circumferentially arranged of smooth muscle cells;

III.tunica adventitia contains loose connective tissue, blood vessels and nerves.

Muscular veins with strong development of muscular elements.

The muscular veins with strong development of muscular elements are below the level of the heart.**These veins contain well developed bundles of smooth muscle cells in all three tunics: in intima and adventitia bundles have a longitudinal direction, and on the media - circular.** There are numerous valves. **Valves consist** of two semilunar folds of the tunica intima that project into the lumen. They are composed of elastic connective tissue and are lined on both sides by endothelium.

I. **tunica intima** forms the valves and consists of:

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer contains loose connective tissue and **bundles** ***longitudinal smooth muscle cells***

II**. tunica media** consists of few layers of ***circular smooth muscle cells;***

III.tunica adventitia contains loose connective tissue *and* ***bundles longitudinal smooth muscle cells***

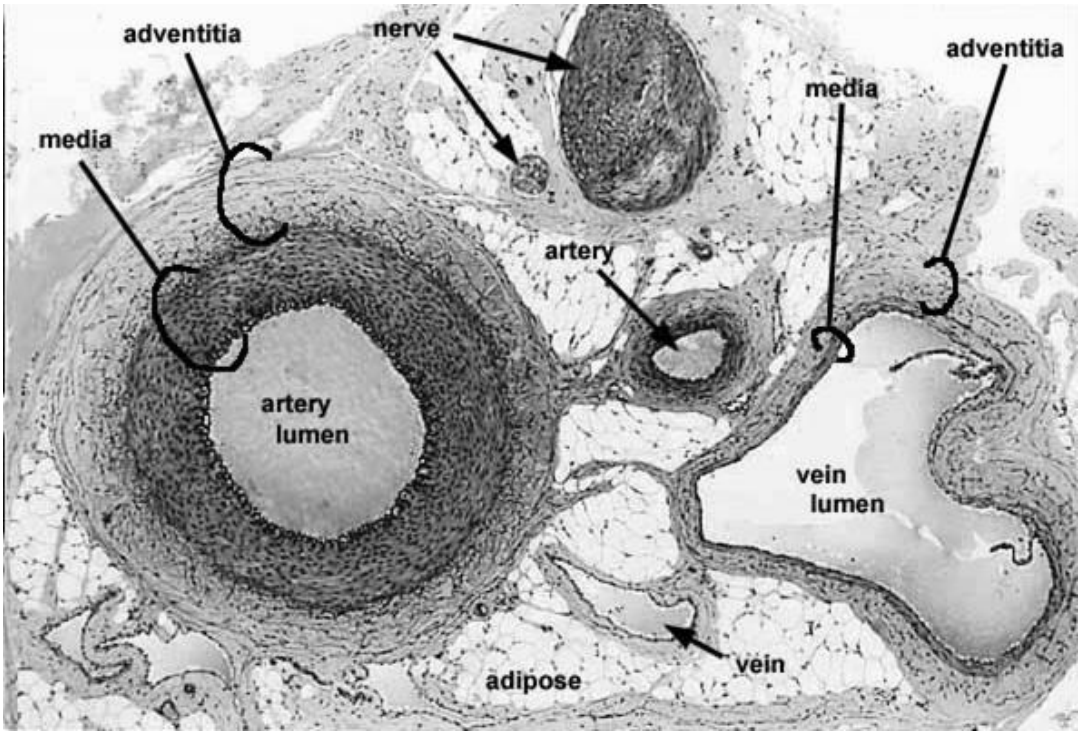


Figure 47. Vascular nerve bundle.

Venules .The venules have very thin walls:

Ⅰ.tunica intima consists of

1) endothelium is simple squamous epithelium, located on the **basement membrane.**

2) subendothelial layer is very thin, consists of loose connective tissue.

Ⅰ Ⅰ.tunica media composed **of one or two circularly arranged layers of smooth muscle cells**.

Ⅰ Ⅰ Ⅰ.tunica adventitia consists of loose connective tissue.

Functions of venules:

1. ***depot of blood***
2. ***blood drainage***
3. ***migration and recirculation of leukocytes***

Capillaries The capillaries are microscopic vessels with diameter of about 8 pm. They branch and anastomose to form a diffuse network. Capillaries have structure to permit metabolic exchange between blood and surrounding tissues.

General structure of capillaries

Capillaries are composed of (fig.54):

I. single layer of polygonal endothelial cells; external surface of endothelial cells rest on the basal lamina;

II. **tunica media** pericytes are cells with long cytoplasmic processes that partly surround the endothelial cells; pericytes have contractile function.

III. **III.tunica adventitia** consists thin layer of loose connective tissue.

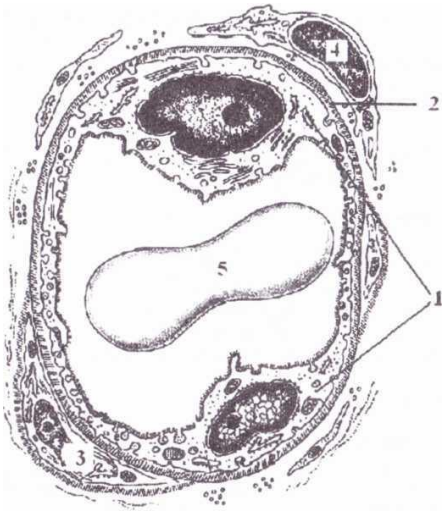


Figure 48.Structure of capillary. 1 - endothelial cell, 2 - basal lamina, 3 - pericytes, 4 - adventitial cell, 5 – erythrocyte.

There are 3 main types of capillaries (fig. 49):

- **Continuous, or somatic**, diameter 7-7.5 pm, capillaries have uninterrupted lining of endothelial cells and basal lamina (fig. 49-1);

Distribution all kinds of muscle tissue, connective tissue, exocrine glands, nervous tissue.

- **Fenestrated, or visceral**, diameter 7-7.5 pm, capillaries have large fenestrae that are closed by a diaphragm; a continuous basal lamina is present (fig. 49-2). Distribution, endocrine glands, glomerulus of kidney.
- **Discontinuous sinusoidal capillaries** have wide diameter (30-40 pm). The endothelial wall is discontinuous, and endothelial cells show multiple fenestrations (fig. 49-3), without diaphragms; the basal lamina is discontinuous. Distribution, the liver, hematopoietic organs such as red bone marrow and spleen.

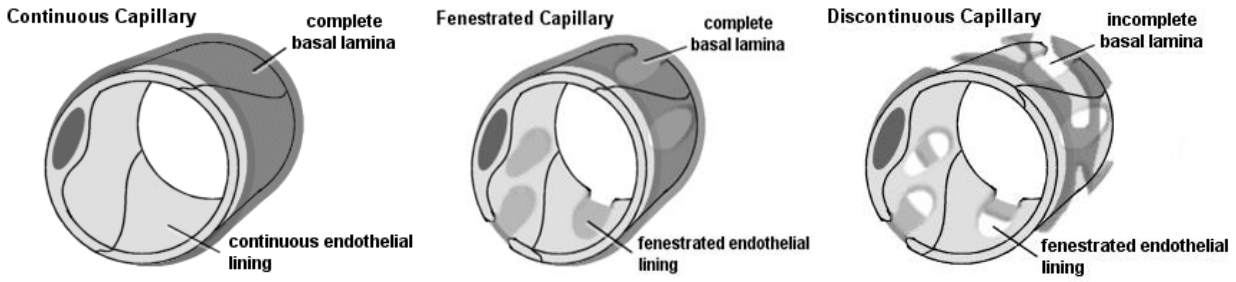


Figure 49. Types of capillaries. I - continuous (somatic) capillary, II - fenestrated (visceral) capillary, III - discontinuous sinusoidal capillary.

Lymphatic vascular system. Lymphatic vascular system consists of endothelium-lined thin- walled channels that collect fluid from the tissue spaces and return it to the blood. This fluid is called lymph, it circulate in only one direction - toward the heart. Three types of lymph vessels can be distinguished based on their size and morphology.

Lymphatic capillaries begin as blind-ending tubes in connective tissue (fig. 50). The basal lamina is absent and the endothelial cells do not form tight junctions, which facilitates the entry of liquids into the lymph capillary. Temporary openings in the endothelial lining of the lymph capillaries also allow the entry of larger particles into the lymph capillaries. Collagen filaments (anchoring filaments) link the endothelium to the surrounding tissue preventing collapse of the lymphatic lumen.

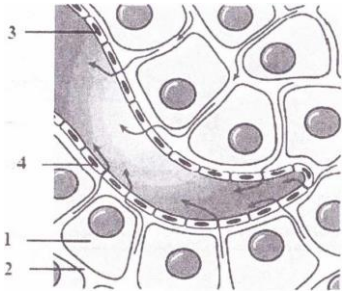


Figure 50. Schematic diagram of a lymphatic capillary. 1 - tissue cell, 2 - tissue fluid, 3 - wall of lymphatic capillary, 4 - opening into lymph vessel

Lymphatic collecting vessels (fig.51) are formed in the result of the fusion of some lymphatic capillaries, have the same structure as the **muscular veins with weak development of muscular elements**. The lymphatic vessels form valves.

The lymph is moved by the compression of the lymph vessels by surrounding tissues. The direction of lymph flow is determined by the valves. Lymph vessels empty intermittently into lymph nodes from which the lymph continues in efferent lymph vessels.

Lymphatic ducts contain one or two layers of smooth muscle cells in their wall, , have the same structure as the **muscular veins with strong development of muscular elements.** They also form **nine half-moon valves**. Peristaltic contractions of the smooth muscle contribute to the movement of lymph towards the heart in addition to the compression of the ducts by surrounding tissues.

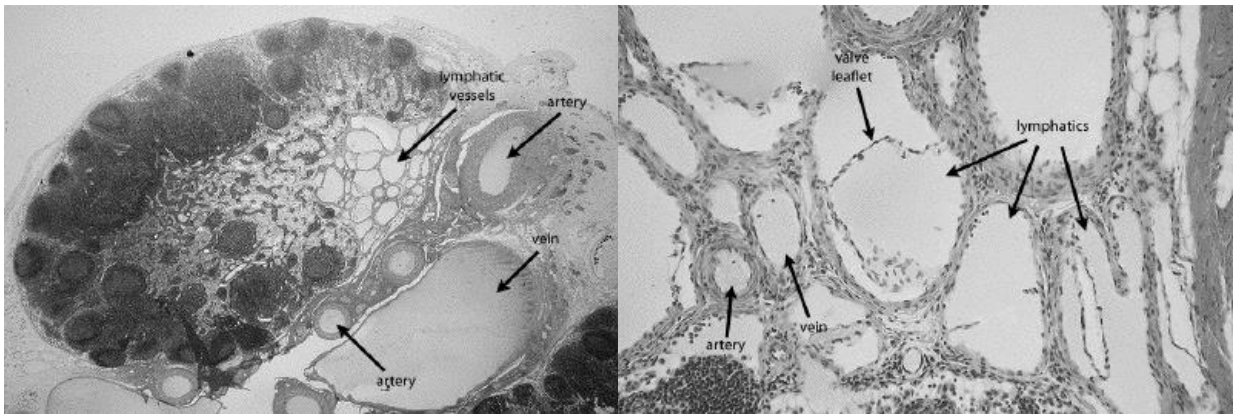


Figure 51A,B. Lymphatic vessels.

Heart.The heart is a muscular organ that contracts rhythmically, pumping the blood through the circulatory system. It is also responsible for producing a hormone called atrial natriuretic factor. **The heart wall consists of 3 tunics** (fig. 58):

I**. Endocardium consists** of:

1) **endothelial cells** is simple squamous epithelium located on the **basement membrane.**

2**) subendothelial layer** of loose connective tissue, in this layer of the endocardium there are normally no blood vessels. Blood supply of the first and second layer of the endocardium is carried out at the expense of blood located in the chambers of the heart. If there are vessels in this layer, then this means that this person became ill with an endocarditis.

3**) muscular-elastic layer** - formed by smooth myocytes and elastic fibers.

4) **external connective tissue layer** includes blood vessels that provide blood supply to the third and fourth layers of the endocardium.

Between the endocardium and the myocardium is a connective tissue subendocardial layer, which consists of veins, nerves, and branches of Purkinje cells.

II.**Myocardium** is the thickest and consists of cardiac muscle cells (fig.52).

IV. **Epicardium** is the serous covering of the heart, forming visceral layer of the pericardium. It is covered by simple squamous epithelium (mesothelium) supported by a thin layer of connective tissue.

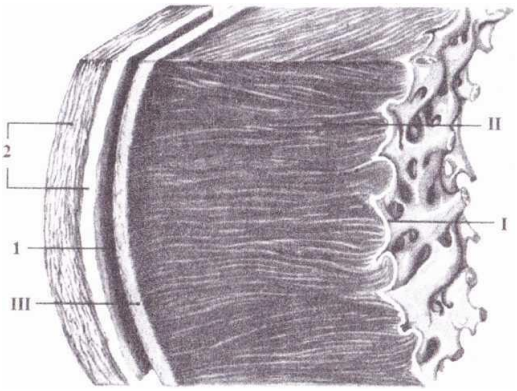


Figure 52. Wall of the heart. I - endocardium, II - myocardium, III - epicardium, 1 - space, 2 – pericardium.

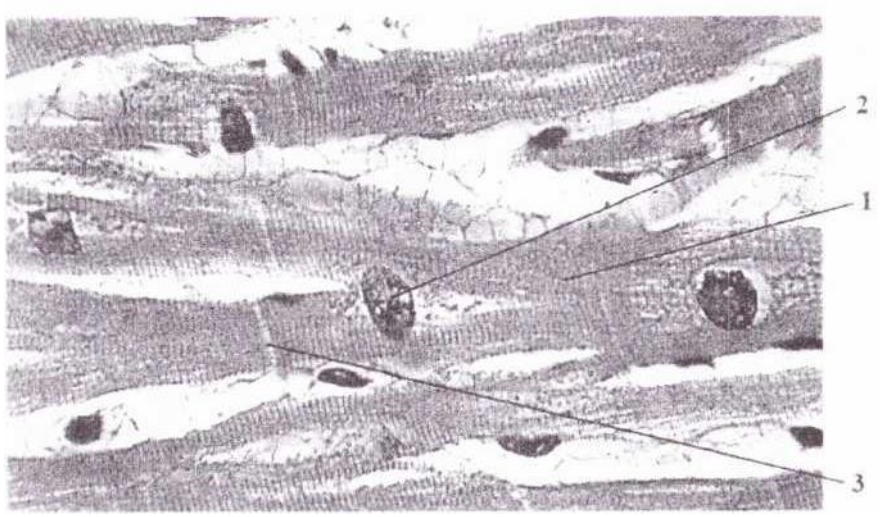


Figure 53. Photomicrograph of the myocardium. 1 - cardiac muscle cells, 2 - nucleus of cardiac muscle cell, 3 - intercalated disk.

There are 3 types of the cardiac muscle cells:

1**) contractile** (ordinary, working);
2) **conductive**;
3) **secretory** (endocrine).

Contractile cardiac cells form the basic part of a myocardium and are characterized highly developed contractile system (fig. 53)

Contractile cardiac muscle - heart muscle, striated, cells may be branched. Cardiac muscle cells are either mono- or binucleate cells. They are connected with one and other by specialized junctional complexes called intercalated disks. Cardiac muscle is capable of involuntary, strong, rhythmic contractions. Recall that cardiac muscle shares a few characteristics with both skeletal muscle and smooth muscle, but it has some unique properties of its own. Not the least of these exceptional properties is its ability to initiate an electrical potential at a fixed rate that spreads rapidly from cell to cell to trigger the contractile mechanism. This property is known as **autorhythmicity**. Neither smooth nor skeletal muscle can do

this. Even though cardiac muscle has autorhythmicity, heart rate is modulated by the endocrine and nervous systems.

There are two major types of cardiac muscle cells: myocardial contractile cells and myocardial conducting cells. The **myocardial contractile cells** constitute the bulk (99 percent) of the cells in the atria and ventricles. Contractile cells conduct impulses and are responsible for contractions that pump blood through the body. The **myocardial conducting cells** (1 percent of the cells) form the conduction system of the heart. Except for Purkinje cells, they are generally much smaller than the contractile cells and have few of the myofibrils or filaments needed for contraction. Their function is similar in many respects to neurons, although they are specialized muscle cells. Myocardial conduction cells initiate and propagate the action potential (the electrical impulse) that travels throughout the heart and triggers the contractions that propel the blood.

Structure of Cardiac Muscle. Compared to the giant cylinders of skeletal muscle, cardiac muscle cells, or cardiomyocytes, are considerably shorter with much smaller diameters. Cardiac muscle also demonstrates striations, the alternating pattern of dark A bands and light I bands attributed to the precise arrangement of the myofilaments and fibrils that are organized in sarcomeres along the length of the cell (Figure 54a). These contractile elements are virtually identical to skeletal muscle. T (transverse) tubules penetrate from the surface plasma membrane, the sarcolemma, to the interior of the cell, allowing the electrical impulse to reach the interior. The T tubules are only found at the Z discs, whereas in skeletal muscle, they are found at the junction of the A and I bands. Therefore, there are one-half as many T tubules in cardiac muscle as in skeletal muscle. In addition, the sarcoplasmic reticulum stores few calcium ions, so most of the calcium ions must come from outside the cells. The result is a slower onset of contraction. Mitochondria are plentiful, providing energy for the contractions of the heart. Typically, cardiomyocytes have a single, central nucleus, but two or more nuclei may be found in some cells.

Cardiac muscle cells branch freely. A junction between two adjoining cells is marked by a critical structure called an intercalated disc, which helps support the synchronized contraction of the muscle (Figure 54b). The sarcolemmas from adjacent cells bind together at the intercalated discs. They consist of desmosomes, specialized linking proteoglycans, tight junctions, and large numbers of gap junctions that allow the passage of ions between the cells and help to synchronize the contraction (Figure 54c). Intercellular connective tissue also helps to bind the cells together. The importance of strongly binding these cells together is necessitated by the forces exerted by contraction.

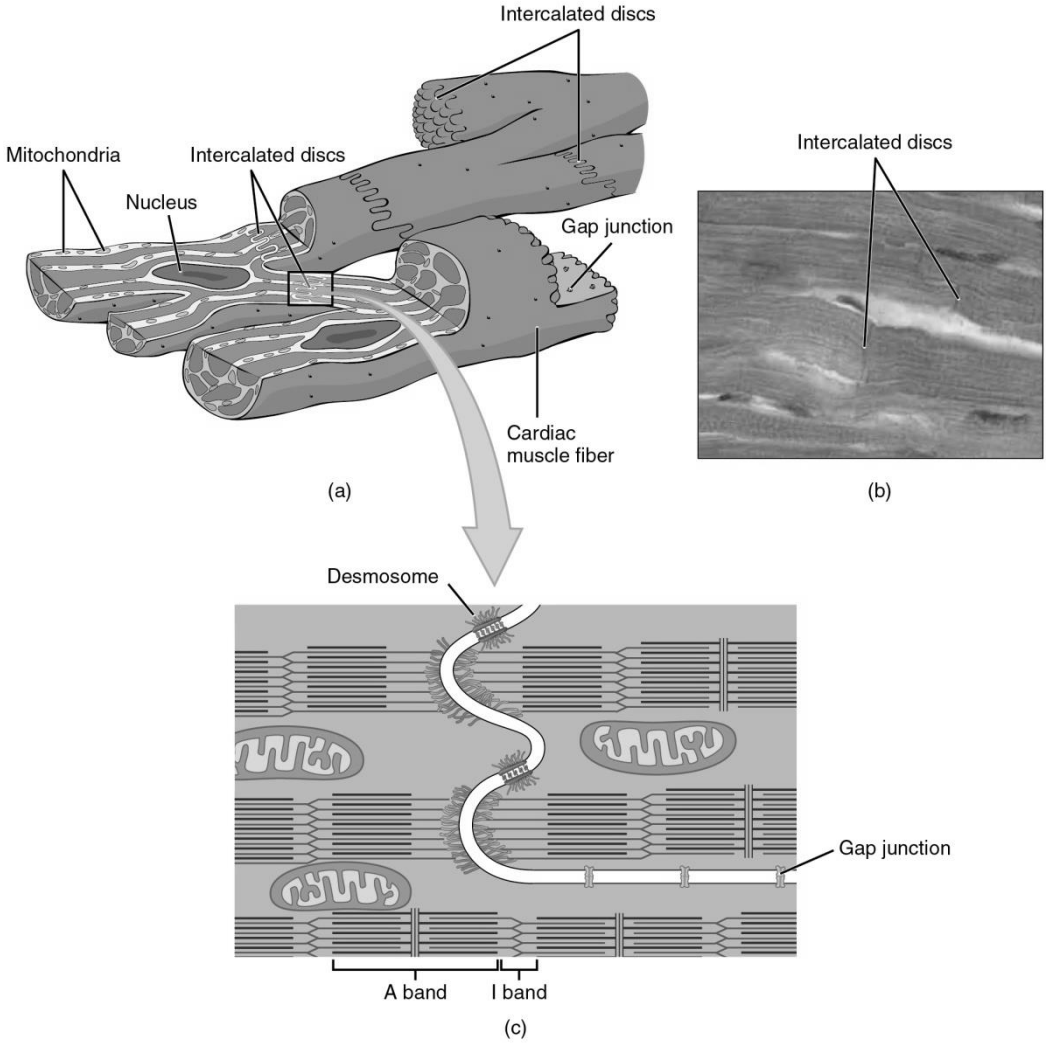


Figure 54. Cardiac Muscle. (a) Cardiac muscle cells have myofibrils composed of myofilaments arranged in sarcomeres, T tubules to transmit the impulse from the sarcolemma to the interior of the cell, numerous mitochondria for energy, and intercalated discs that are found at the junction of different cardiac muscle cells. (b) A photomicrograph of cardiac muscle cells shows **the** nuclei and intercalated discs. (c) An intercalated disc connects cardiac muscle cells and consists of desmosomes and gap junctions. LM × 1600. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

Cardiac muscle undergoes aerobic respiration patterns, primarily metabolizing lipids and carbohydrates. Myoglobin, lipids, and glycogen are all stored within the cytoplasm. Cardiac muscle cells undergo twitch-type contractions with long refractory periods followed by brief relaxation periods. The relaxation is essential so the heart can fill with blood for the next cycle. The refractory period is very long to prevent the possibility of tetany, a condition in which muscle remains involuntarily contracted. In the heart, tetany is not compatible with life, since it would prevent the heart from pumping blood. **Damaged cardiac muscle** cells have extremely limited abilities to repair themselves or to replace dead cells via mitosis. Recent evidence indicates that at least some stem cells remain within the heart that continue to divide and at least potentially replace these dead cells. However, newly formed or repaired cells are rarely as functional as the original cells, and cardiac

function is reduced. In the event of a heart attack or MI, dead cells are often replaced by patches of scar tissue. Autopsies performed on individuals who had successfully received heart transplants show some proliferation of original cells. If researchers can unlock the mechanism that generates new cells and restore full mitotic capabilities to heart muscle, the prognosis for heart attack survivors will be greatly enhanced. To date, myocardial cells produced within the patient (*in situ*) by cardiac stem cells seem to be nonfunctional, although those grown in Petri dishes (*in vitro*) do beat. Perhaps soon this mystery will be solved, and new advances in treatment will be commonplace.

Conductive cardiac ceils (fig.55) have ability to generation and conduction of electrical impulses through an impulse-generating and impulseconducting system of heart. **There are 2 types of conductive cardiac cells**:

- **pacemaker (nodal) cells** or P-cells are the modified cardiac muscle cells with pale cytoplasm and fewer myofilaments; these cells are situated in the sinoatrial, atrioventricular nodes and internodal tracts.
- **Purkinje fibers** form atrioventricular bundle of His. Purkinje fibers are modified cardiac muscle cells found in the subendocardium of the ventricles. They constitute part of the specialized impulse conducting system, which connects to the right and left bundle branches and regulates the heartbeat. These are large muscular cells with a vacuolated cytoplasm due to the high glycogen content. Other characteristics that help distinguish Purkinje fibers from typical cardiac muscle cells are that they contain fewer myofibrils, and more sarcoplasm. The bundles of Purkinje cells travel in the subendocardial layer to the apex of the heart, where they being giving off side branches that make contact with working cells.

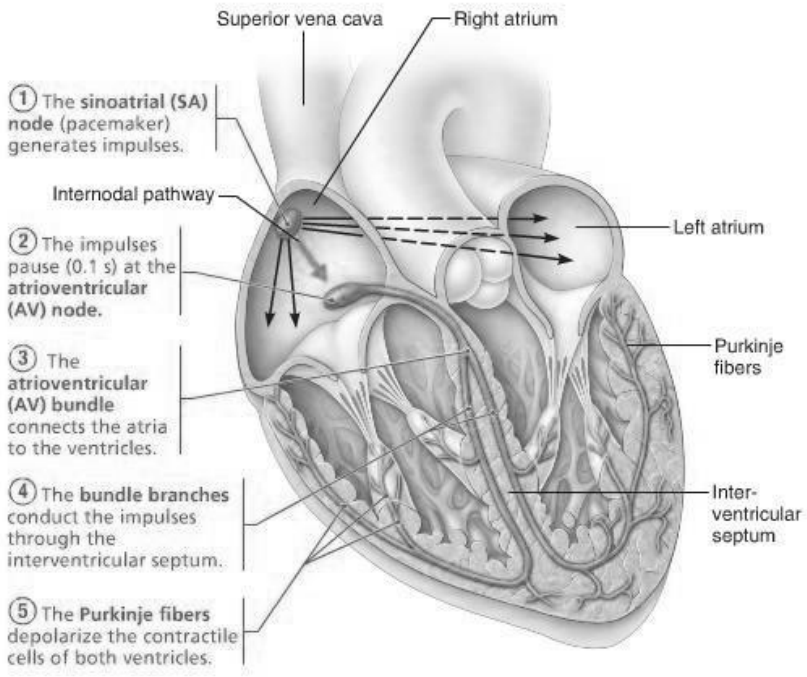


Figure 55. Conduction System of the Heart.

If embryonic heart cells are separated into a Petri dish and kept alive, each is capable of generating its own electrical impulse followed by contraction. When two independently beating embryonic cardiac muscle cells are placed together, the cell with the higher inherent rate sets the pace, and the impulse spreads from the faster to the slower cell to trigger a contraction. As more cells are joined together, the fastest cell continues to assume control of the rate. A fully developed adult heart maintains the capability of generating its own electrical impulse, triggered by the fastest cells, as part of the cardiac conduction system. The components of the cardiac conduction system include the sinoatrial node, the atrioventricular node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje cells (Figure 55).

Sinoatrial (SA) Node

Normal cardiac rhythm is established by the **sinoatrial (SA) node**, a specialized clump of myocardial conducting cells located in the superior and posterior walls of the right atrium in close proximity to the orifice of the superior vena cava. The SA node has the highest inherent rate of depolarization and is known as the **pacemaker** of the heart. It initiates the **sinus rhythm**, or normal electrical pattern followed by contraction of the heart.

This impulse spreads from its initiation in the SA node throughout the atria through specialized **internodal pathways**, to the atrial myocardial contractile cells and the atrioventricular node. The internodal pathways consist of three bands (anterior, middle, and posterior) that lead directly from the SA node to the next node in the conduction system, the atrioventricular node (see Figure 56). The impulse takes approximately 50 ms (milliseconds) to travel between these two nodes. The relative importance of this pathway has been debated since the impulse would reach the atrioventricular node simply following the cell-by-cell pathway through the contractile cells of the myocardium in the atria. In addition, there is a specialized pathway called **Bachmann's bundle** or the **interatrial band** that conducts the impulse directly from the right atrium to the left atrium. Regardless of the pathway, as the impulse reaches the atrioventricular septum, the connective tissue of the cardiac skeleton prevents the impulse from spreading into the myocardial cells in the ventricles except at the atrioventricular node. Figure 56 illustrates the initiation of the impulse in the SA node that then spreads the impulse throughout the atria to the atrioventricular node.

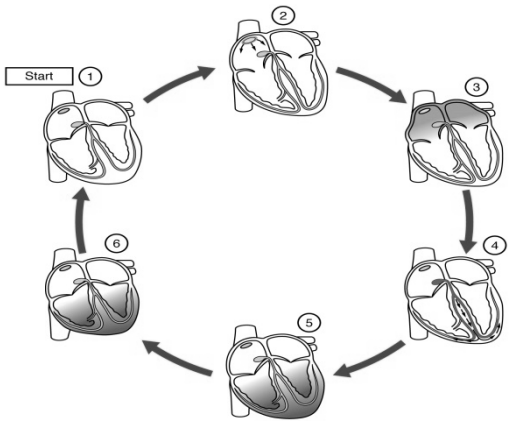


Figure 56. Cardiac Conduction. (1) The sinoatrial (SA) node and the remainder of the conduction system are at rest. (2) The SA node initiates the action potential, which sweeps across the atria. (3) After reaching the atrioventricular node, there is a delay of approximately 100 ms that allows the atria to complete pumping blood before the impulse is transmitted to the atrioventricular bundle. (4) Following the delay, the impulse travels through the atrioventricular bundle and bundle branches to the Purkinje fibers, and also reaches the right papillary muscle via the moderator band. (5) The impulse spreads to the contractile fibers of the ventricle. (6) Ventricular contraction begins.

The electrical event, the wave of depolarization, is the trigger for muscular contraction. The wave of depolarization begins in the right atrium, and the impulse spreads across the superior portions of both atria and then down through the contractile cells. The contractile cells then begin contraction from the superior to the inferior portions of the atria, efficiently pumping blood into the ventricles.

Atrioventricular (AV) Node

The **atrioventricular (AV) node** is a second clump of specialized myocardial conductive cells, located in the inferior portion of the right atrium within the atrioventricular septum. The septum prevents the impulse from spreading directly to the ventricles without passing through the AV node. There is a critical pause before the AV

node depolarizes and transmits the impulse to the atrioventricular bundle (see Figure 56, step 3). This delay in transmission is partially attributable to the small diameter of the cells of the node, which slow the impulse. Also, conduction between nodal cells is less efficient than between conducting cells. These factors mean that it takes the impulse approximately 100 ms to pass through the node. This pause is critical to heart function, as it allows the atrial cardiomyocytes to complete their contraction that pumps blood into the ventricles before the impulse is transmitted to the cells of the ventricle itself. With extreme stimulation by the SA node, the AV node can transmit impulses maximally at 220 per minute. This establishes the typical maximum heart rate in a healthy young individual. Damaged hearts or those stimulated by drugs can contract at higher rates, but at these rates, the heart can no longer effectively pump blood.

Atrioventricular Bundle (Bundle of His), Bundle Branches, and Purkinje Fibers

Arising from the AV node, the **atrioventricular bundle**, or **bundle of His**, proceeds through the interventricular septum before dividing into two **atrioventricular bundle branches**, commonly called the left and right bundle branches. The left bundle branch has two fascicles. The left bundle branch supplies the left ventricle, and the right bundle branch the right ventricle. Since the left ventricle is much larger than the right, the left bundle branch is also considerably larger than the right. Portions of the right bundle branch are found in the moderator band and supply the right papillary muscles. Because of this connection, each papillary muscle receives the impulse at approximately the same time, so they begin to contract simultaneously just prior to the remainder of the myocardial contractile cells of the ventricles. This is believed to allow tension to develop on the chordae tendineae prior to right ventricular contraction. There is no corresponding moderator band on the left. Both bundle branches descend and reach the apex of the heart where they connect with the Purkinje fibers (see Figure 56, step 4). This passage takes approximately 25 ms.

The **Purkinje fibers** are additional myocardial conductive fibers that spread the impulse to the myocardial contractile cells in the ventricles. They extend throughout the myocardium from the apex of the heart toward the atrioventricular septum and the base of the heart. The Purkinje fibers have a fast inherent conduction rate, and the electrical impulse reaches all of the ventricular muscle cells in about 75 ms (see Figure 56, step 5). Since the electrical stimulus begins at the apex, the contraction also begins at the apex and travels toward the base of the heart, similar to squeezing a tube of toothpaste from the bottom. This allows the blood to be pumped out of the ventricles and into the aorta and pulmonary trunk. The total time elapsed from the initiation of the impulse in the SA node until depolarization of the ventricles is approximately 225 ms.

Secretory (endocrine) cardiac cells are found in atrial cells and are characterized by weak development of contractile system. In their sarcoplasm near to poles of a nucleus there are granules containing hormone (atrial natriuretic factor, auriculin, or atriopeptin).

Cardiac skeleton.The cardiac skeleton is comprised of dense connective tissue that encircles the base of the two arteries leaving the heart and the openings between the chambers. It serves as an attachment for cardiac muscle and the cuspid valves of the atria and ventricles. It also serves as an attachment site for the semi lunar valves of the aorta and the pulmonary artery. The atrioventricular (AV) bundle passes from the right atrium to the ventricular septum via the fibrous skeleton. **The cardiac skeleton consists of dense connective tissue arranged into:**

1) 4 fibrous rings which surround the valve orifices;
2) 2 fibrous trigones connecting the fibrous rings;
3) membranous part of interventricular and interatrial septa.

Heart valves .The heart valves are composed of three layers:

- **fibrosa** forms the core of the valve and consists of dense irregular connective tissue of skeletal rings of the heart;
- **spongiosa** is formed by loose connective tissue located on the atrial and/or blood vessel side of each valve; it serves as the shock absorber;
- **ventricularis** is the part adjacent to the ventricular and/or atrial surface of each valve, is covered with endothelium; the outside extends into the fibrous cap on the tips of the papillary muscles.

Development of the heart and blood vessels. **Distinguish 5 stages to heart development.**

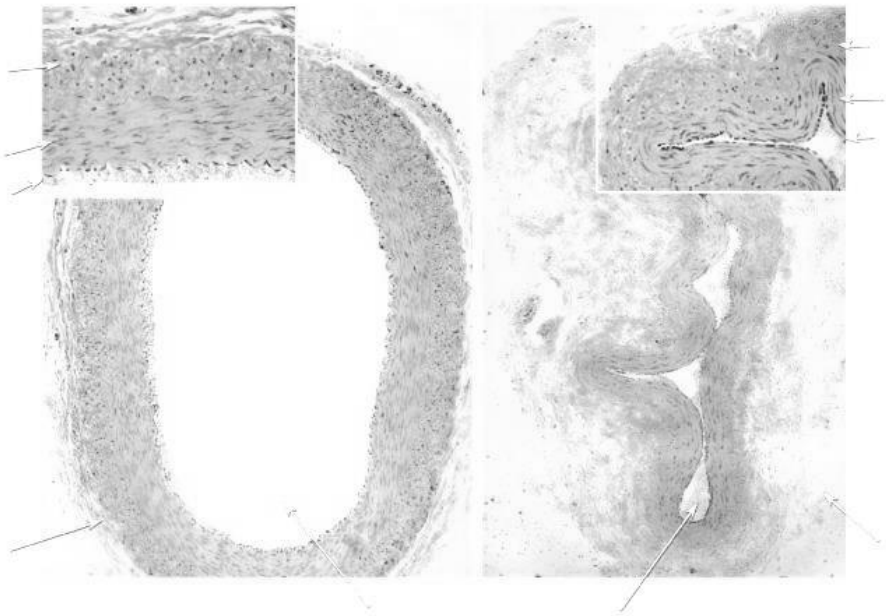
- Specification of cardiac precursor cells
- Migration of cardiac precursor cells and fusion of the primodia
- Heart looping
- Heart chamber formation
- Septation and valve formation

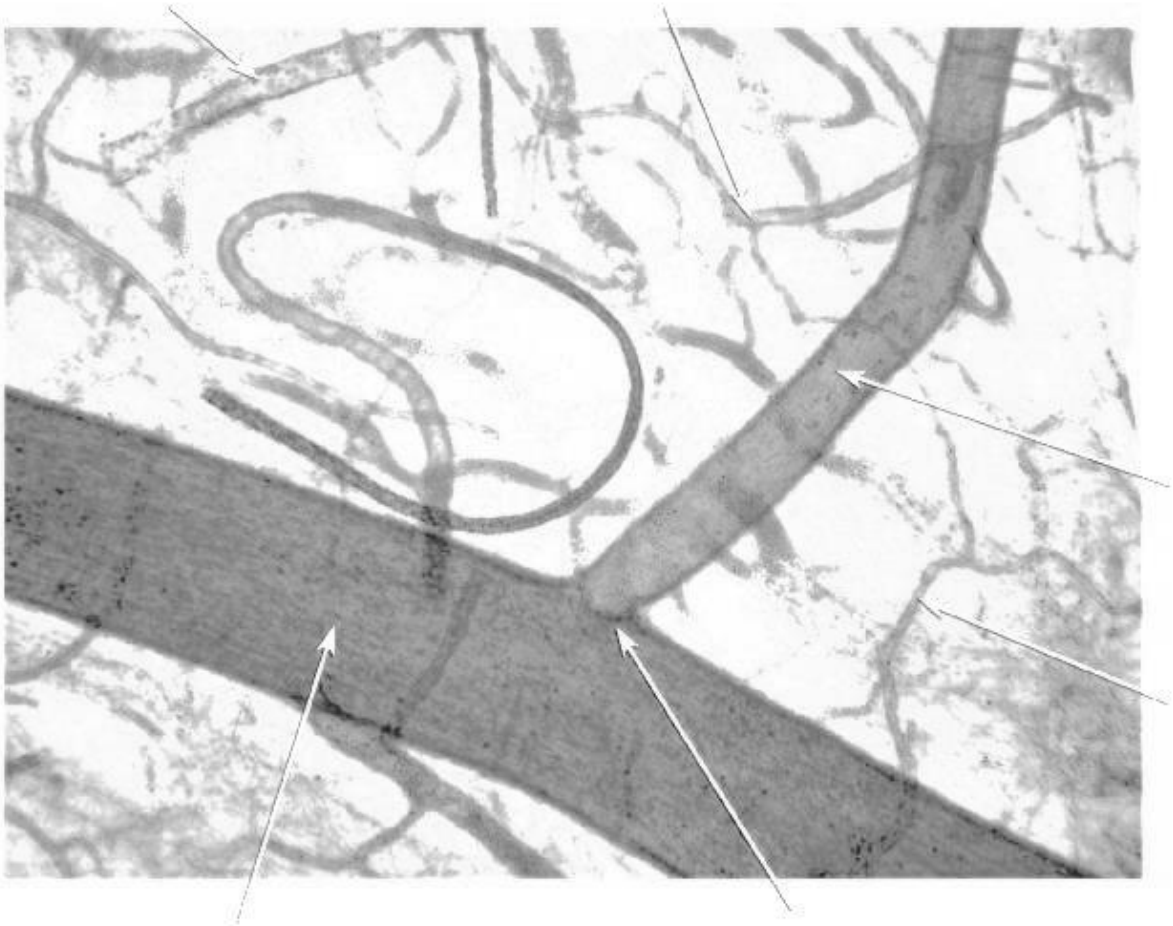
The primordium of the heart forms in the cardiogenic plate (the part of the splanchnopleuric mesoderm) located at the cranial end of the embryo. Angiogenic cell clusters which lie in a horse-shoe shape configuration in the plate coalesce to form two endocardial tubes. These tubes are then forced into the thoracic region due to cephalic and lateral foldings where they fuse together forming a single endocardial tube. The tube can be subdivided into primordial heart chambers starting caudally at the inflow end: the sinus venosus, primitive atria, ventricle, and bulbus cordis. The heart tube begins to grow rapidly forcing it to bend upon itself. The result is the bulboventricular loop. Septa begin to grow in the atria, ventricle and bulbus cordis to form right and left atria, right and left ventricles and two great vesselsthe pulmonary artery and the aorta. By the end of the eighth week partitioning is completed and the fetal heart has formed.

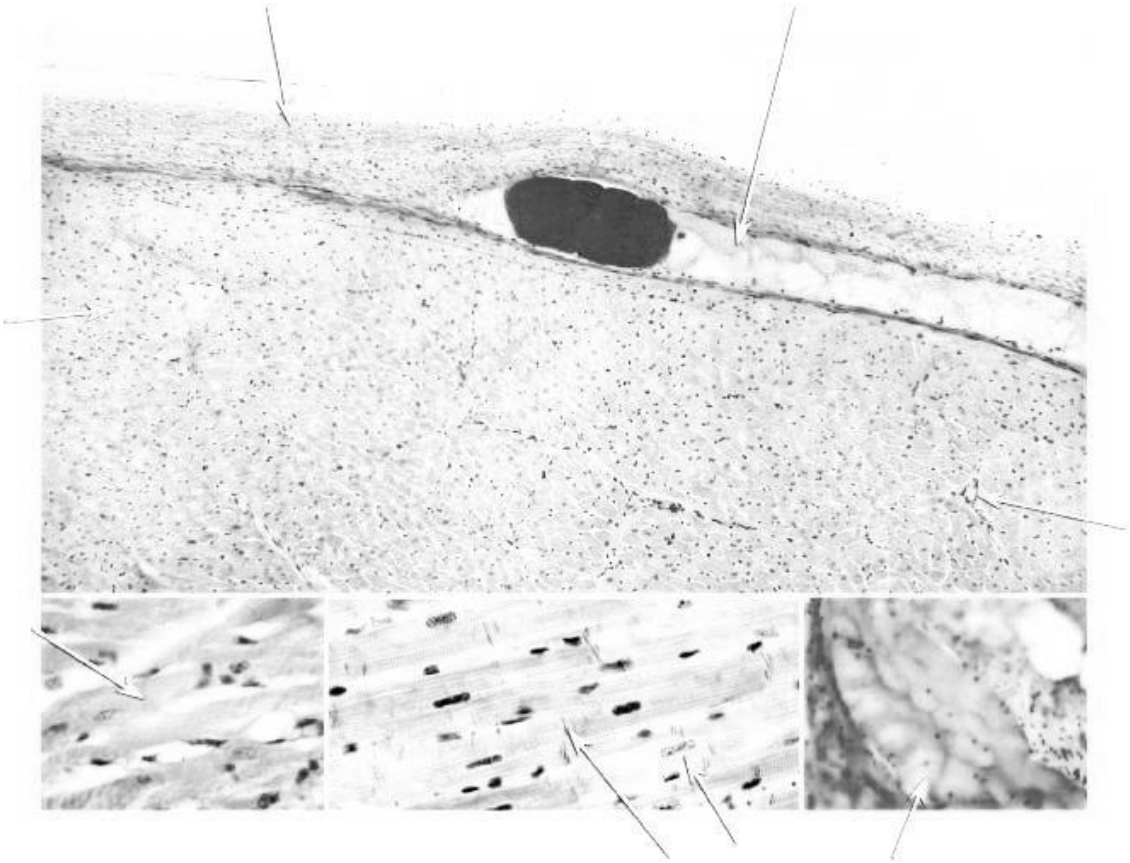
Practical lessons

1. Vessels classification. Structure and functions of the arteries.
2. Strucutre, classification and functions of the veins.
3. Microcirculatory bed. Classification, structure and functions of the capillaries.
4. Lymphatic system. The structure and function of the lymphatic vessels.
5. Heart tunices: their structure and functions.
6. Heart. Peculiaraities of the heart conductive system (structure and function).

Paint and mark basic histological structure







Signature of teacher_____

CENTRAL (PRIMARY) LYMPHOID ORGANS CENTRAL (PRIMARY) LYMPHOID ORGANS

The central or primary lymphoid organs generate lymphocytes from immature progenitor cells. The thymus and the bone marrow constitute the primary lymphoid tissues involved in the production and early selection of lymphocytes. The secondary lymphoid organs include the lymph nodes, spleen, and small masses of lymph tissue such as Peyer's patches, the appendix, tonsils, and the mucosa-associated lymphoid tissue (MALT). The secondary lymphoid organs serve two basic functions: they are a site of further lymphocyte maturation, and they efficiently trap antigens for exposure to T and B cells.

Red bone marrow. The red bone marrow is found mainly in the flat bones, such as the hip bone, breast bone, skull, ribs, vertebrae and shoulder blades, and in the cancellous material at the epiphyseal ends of the long bones such as the femur and humerus.

Functions of red bone marrow

1. Production of myeloid and lymphoid blood cells.
2. Proliferation and antigen-independent differentiation of B- lymphocyte (red bone marrow is the mammalian equivalent of the bursa of Fabricius of birds).
3. Storage in macrophages of iron derived from the breakdown of hemoglobin.
4. Destruction of aged and defective blood cells. Structure of red bone marrow

Red bone marrow (fig.57) is composed of 3 main components:

- stroma,
- hematopoietic cords,
- sinusoidal capillaries (sinusoids).

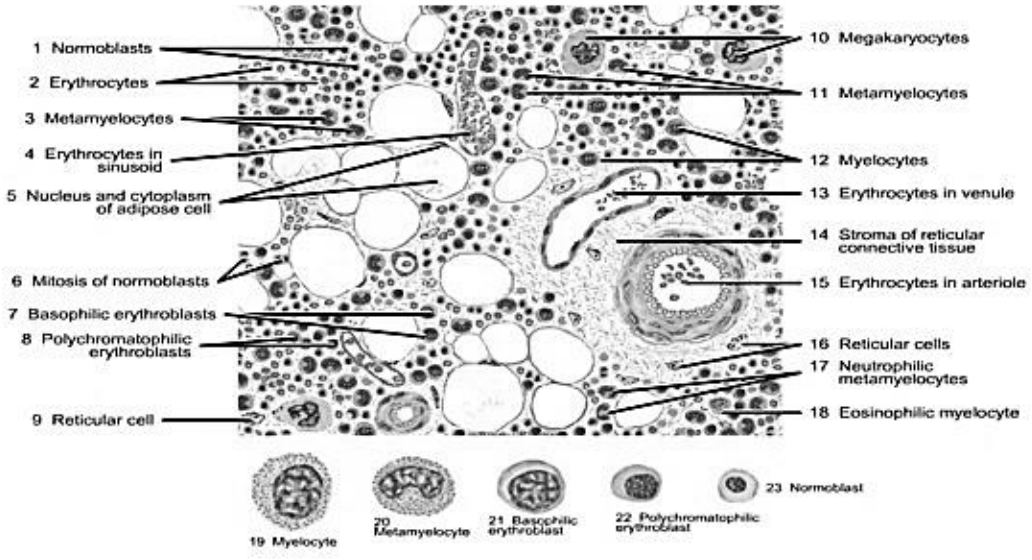


Figure 57. Red bone marrow smear. 1 — erythroid cells, 2 — neutrophilic myelocytes, 3 - early neutrophilic metamyelocyte.

Stroma consists of a three-dimensional meshwork of reticular tissue, which contains reticular cells and reticular fibers, macrophages, adipose cells, cells of endosteum, osteoblasts, osteoclasts, endothelial cells forming the wall of sinusoids. **Hematopoietic component** (**hematopoietic cords**) is formed by the myeloid tissue and contains the myeloid and lymphoid cells at different stages of their development, cooperating with stromal elements. Stroma provides the hematopoietic microenvironment that facilitates hematopoiesis by the generation of colony stimulating factors, affecting hematopoiesis.

There is compartmentalization in the bone marrow, in that certain cell types tend to aggregate in specific areas in nests or clusters. For instance, erythropoietic cells develop in **erythroblastic islets**, in contact with the macrophages which accumulate and transfer them the iron necessary for synthesis of hemoglobin. The erythroblastic island consists of macrophage surrounded by erythrocyte progenitor cells (fig.58).

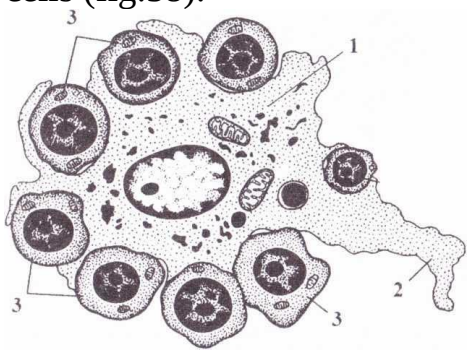


Figure 58. Schematic diagram of erythroblastic islet. 1 - macrophage, 2 — processes of macrophage, 3 - erythropoietic cells.

Megakaryocytes (fig.59) unlike other blood cells, remain in the bone marrow when mature, being extraordinarily large (diameter up to 60 pm), with a highly polyploid nucleus. They normally lie close beside blood sinuses, and they extend processes through holes in the endothelial lining of these vessels; liberating the platelets.

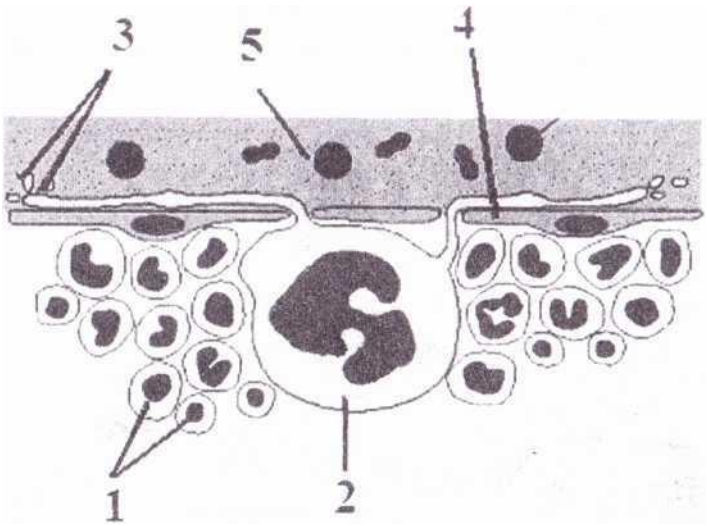


Figure 59. Schematic diagram of megakaryocyte among other cells in the bone marrow. 1 - developing blood cells, 2 - megakaryocyte, 3 - processus of megakaryocyte. 4 - endothelial cells of sinusoid, 5 - lumen of sinusoid

Granulocytes mature near the cells of endosteum and contact with reticular and adipose cells. **Sinusoidal capillaries** are a system of interconnected blood vessels. They are formed by a continuous layer of endothelial cells. Some regions of the endothelium are thin and may be sites for migration of mature cells from the stroma into the sinusoids. The release of mature blood cells from the bone marrow is controlled by releasing factors produced in response to the needs of the organism.

Bone marrow barrier. The biood vessels constitute a barrier, inhibiting immature blood cells from leaving the bone marrow. Only mature blood cells contain the membrane proteins required to attach to and pass the blood vessel endothelium. Hematopoietic stem cells may also cross the bone marrow barrier, and may thus be harvested from blood.

Yellow bone marrow.The yellow bone marrow is located in the hollow centers of the long bones such as in the legs and in the arms, largely consists of fat cells. The yellow bone marrow turns into red marrow in emergencies such as blood loss or anaemia. It would be able to convert itself within 1 - 2 hours to take over the role of a red marrow and this is one of the natural reserves to sustain life in extreme events.

Thymus The thymus is bilobed organ situated above the heart and below the thyroid gland (fig.60)

Functions of the thymus

1. Development of T-lymphocytes derived from bone marrow (proliferation and antigen-independent differentiation of T-lymphocyte).
2. Secretion of hormones which regulate T-cell maturation and proliferation (thymulin, thymopoietin and thymosin alpha 1).
3. Haematopoiesis during fetal development.

Structure of the thymus

The thymus has a connective tissue capsule that penetrates into the parenchyma and divides organ into lobules (fig.60).

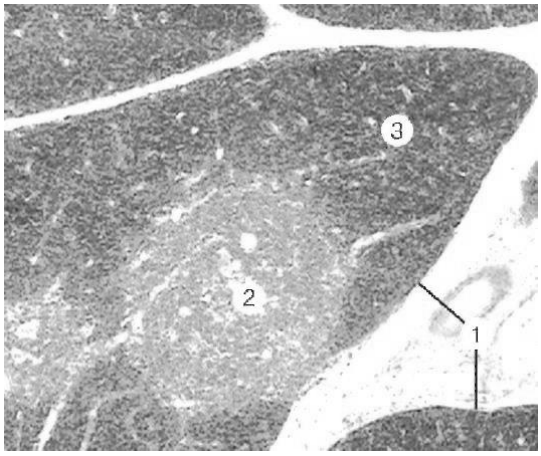


Figure 60. Photomicrograph of human thymus. 1 - lobule, 2 – medulla, 3 – cortex.

The thymus has two tissue components**: parenchyma and stroma**.
The **parenchyma** is composed mostly of T lymphocytes in various stages of development into mature T cells. The **stroma** is composed of special **epithelioreticular supporting cells**, macrophages and thymic interdigitating cells. The epithelial reticular cells are stellate cells with pale oval nuclei (fig.61);

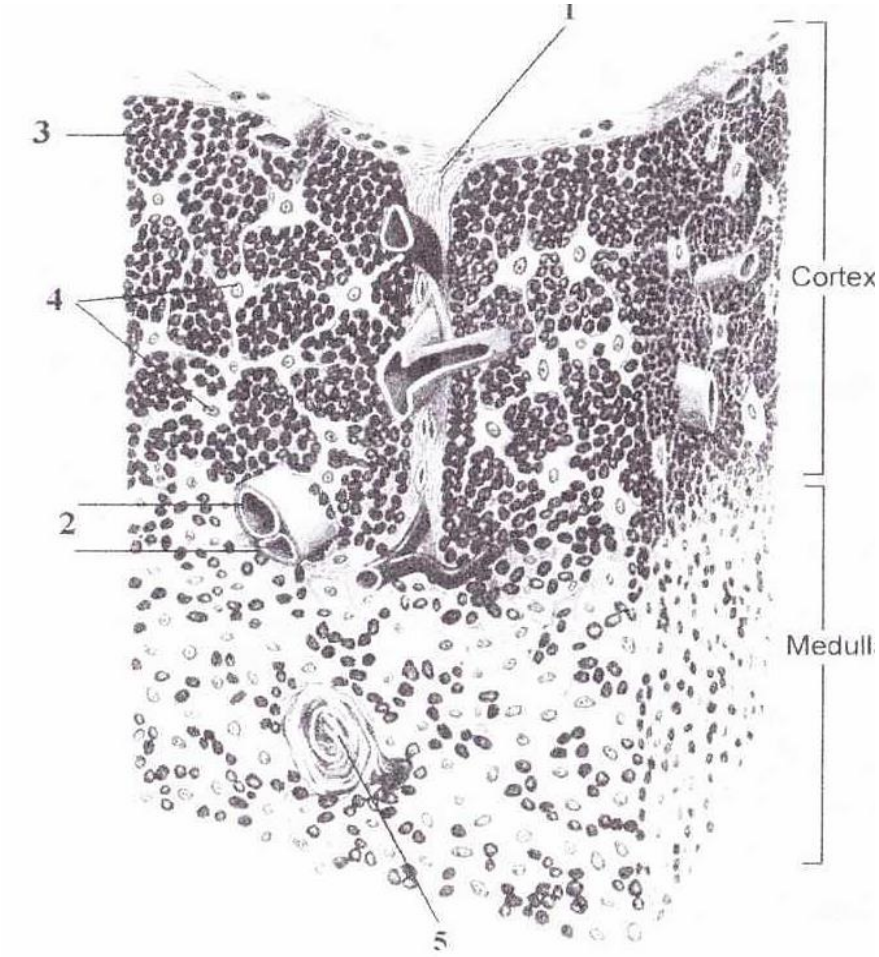


Figure 61. Schematic diagram of thymic lobule. 1 - septum, 2 - blood vessels, 3 — thymocytes, 4 — epithelioreticular cells, 5 — Hassall's corpuscle

cytoplasm contains secretory granules which contain the thymic hormones. These cells are bound together by desmosomes and form extensive network.
Each lobule of the thymus has a **peripheral dark zone (the cortex)** and a **central light zone (the medulla)**. High concentration of T lymphocytes in the cortex is the basis for the intense basophilia of this region and this is the site of precursor cell proliferation and maturation. Mature immunocompetent T cells then move from the cortex toward the medulla where they enter the bloodstream to be taken out of the thymus.
The cortex is composed of densely packed lymphocytes (immature T-lymphocytes or thymocytes), epithelioreticular cells, and few macrophages. Large, dividing thymocytes are present in the most peripheral zone of the cortex. Smaller cells are evident toward the center of cortex.

In the medulla, the stroma consists of prominent epithelioreticular cells that have large, pale-staining nuclei and substantial amounts of eosinophilic cytoplasm. There are fewer T cells because most of them have entered the blood stream via vessels at the corticomedullary junction. Antigen presenting cells (APC) are also found in the medulla where they are called thymic interdigitating cells. These cells are thought to present self-antigens to the matured T cells. T cells that recognize these sell-antigens are removed by a process called apoptosis. This process helps to prevent autoimmune diseases. The medulla also contains **Hassall's corpuscle**

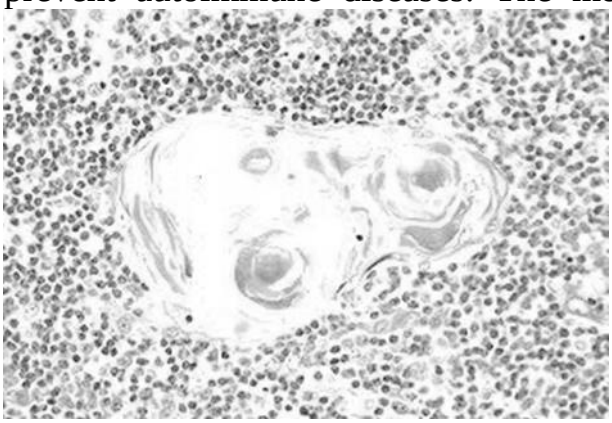


Figure 62. Photomicrograph of human thymus medulla.

These structures are concentrically arranged, flattened epithelioreticular cells that degenerate. Their function is unknown. Blood-thymus barrier The **blood-thymus barrier** regulates exchange of substances between the circulatory system and thymus, providing a sequestered environment for immature T cells to develop.

The barrier also prevents the immature T cells from contacting foreign antigens (since contact with antigens at this stage will cause the T cells to die by apoptosis).

Blood-thymus barrier components:

1) endothelium of a capillary;
2) basal lamina of a capillary endothelium;
3) basal lamina of epithelioreticular cells;
4) epithelioreticular cells.

Development of the thymus. The two main components of the thymus, the thymocytes and the epithelioreticular cells, have distinct developmental origins. The thymic epithelium is the first to develop, and appears in the form of two flaskshape endodermal diverticula, which arise, one on either side, from the third branchial pouch (pharyngeal pouch), and extend lateral and backward into the surrounding mesoderm and neural crest-derived mesenchyme in front of the ventral aorta. Here they meet and become joined to one another by connective tissue, but there is never any fusion of the thymus tissue proper. The pharyngeal opening of each diverticulum is soon obliterated, but the neck of the flask persists for some time as a cellular cord. By further proliferation of the cells lining the flask, buds of cells are formed, which become surrounded and isolated by the invading mesoderm. During the late stages of the development of the thymic epithelium, hematopoietic bone-marrow precursors migrate into the thymus. Normal thymic development thereafter is dependent on the interaction between the thymic epithelium and the hematopoietic thymocytes.

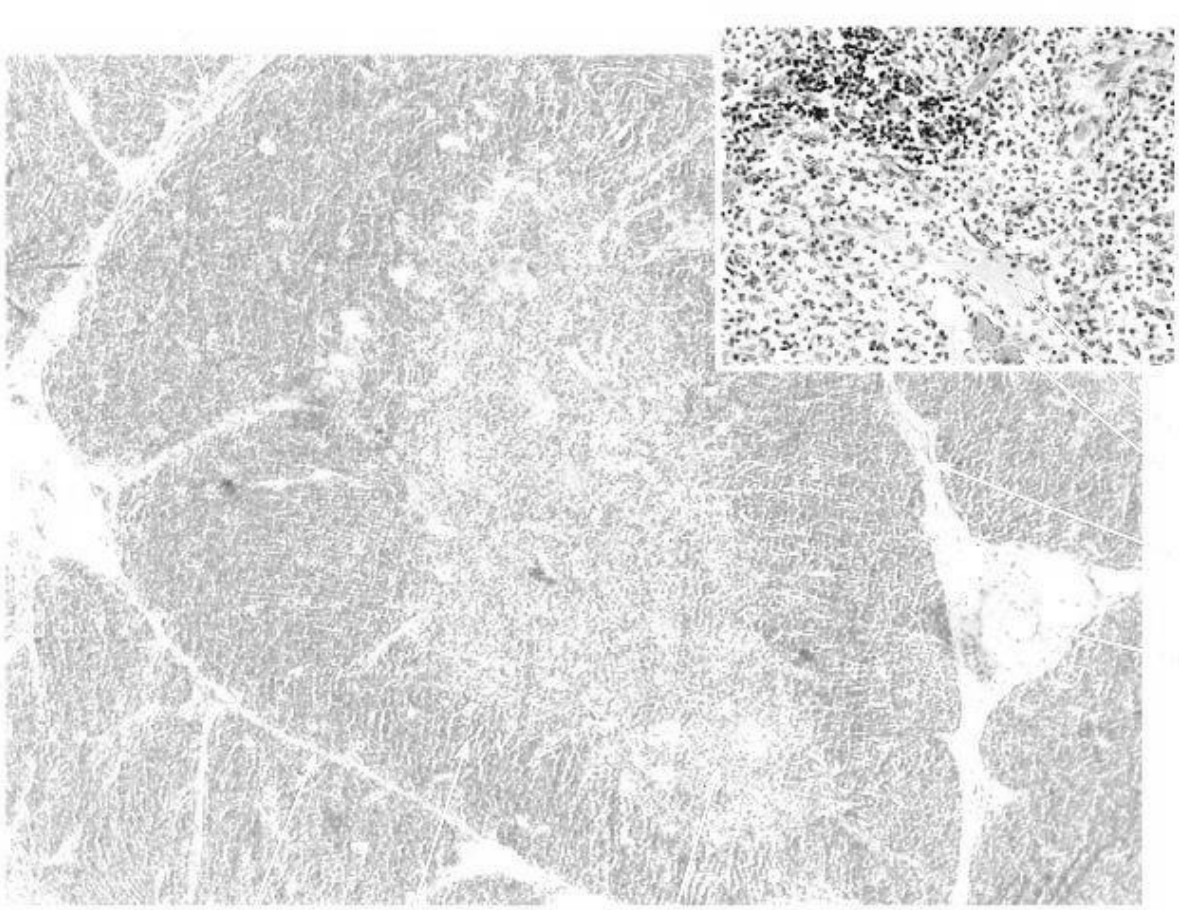
Involution of the thymus

- **Changes with age**. The thymus is relatively large at birth. There is rapid growth until the end of the second year, and then it slows. The maximum size is achieved at puberty (about 35 grams), and then there is a decrease in size through a process known as age involution. There is a replacement of cortical thymocytes with fat, an increase in the number and size of Hassall's corpuscles. The atrophy is due to the increased circulating level of sex hormones. Despite involution, the thymus remains functional throughout life.
- **Acute (stress) involution** may occur in response to severe disease and metabolic stress associated with pregnancy, lactation, infection, surgery, malnutrition, malignancy and other systemic insults. Stress involution is characterized by greatly increased lymphocyte death and is probably mediated by high levels of corticosteroids.
- **Status thymicolymphaticus** hyperplasia of the lymphatic tissue formerly b elieved tobe a cause of sudden death in infancy and childhood but now no lo nger recognized as a genuine pathological entitycalled also lymphatism.

Practical lessons

1. Thymus: structure and functions.
2. Red bone marrow: structure and function.

Paint and mark basic histological structure



Signature of teacher_____

PERIPHERAL (SECONDARY) LYMPHOID ORGANS

Lymph nodes. The lymph nodes are small encapsulated bean-shaped organs composed of lymphoid tissue lying in the path of lymph vessels. They range in size from 1 mm to about 1 to 2 cm in their longest dimension.

Functions of lymph nodes :

1. Non-specific filtration of particulate matter and microorganisms from lymph by the phagocytic activity of macrophages, thus preventing exogenous material from reaching the general circulation.
2. Interaction of circulating lymphocytes with antigen-containing lymph.
3. Aggregation, activation and antigen-dependent proliferation of Blymphocytes in response to antigenic stimulation, plasma cell formation and antibody production.
4. Aggregation, activation and antigen-dependent proliferation of Tlytnphocytes with induction of cytotoxic immune responses after antigenic stimulation.

Structure of the lymph node

The lymph node (fig.68) has a convex side, through which multiple afferent lymphatic vessels enter, and a concave depression, the hilum, through which arteries and nerves enter and veins and efferent lymphatic vessel leave the organ.

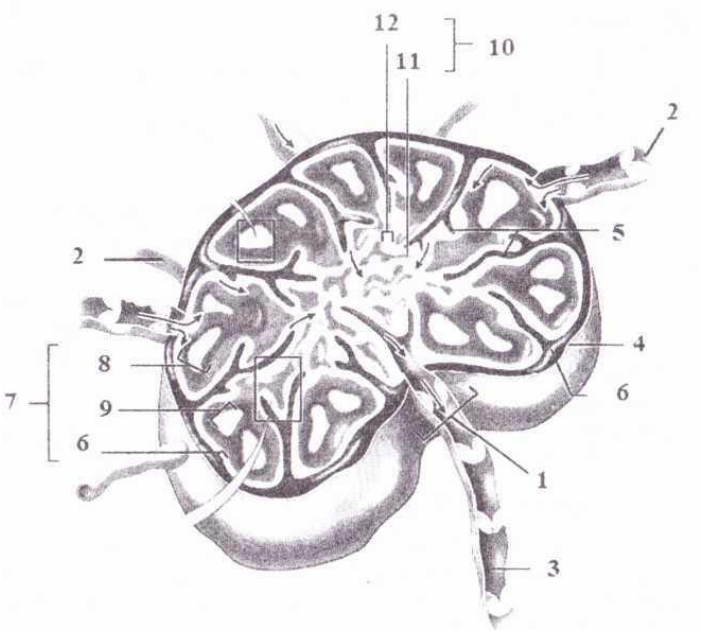


Figure 63. Schematic diagram of lymph node. 1 —hilrnri, 2 - afferent lymphatic vessels, 3 - efferent lymphatic vessel, 4 - capsule, 5 — trabeculae, 6 - subcapsular sinus, 7 - cortex, 8 - lymphatic nodule, 9 — germinal center, 10 — medulla, 11 - medullary cord, 12 - medullary sinus

The lymph node is surrounded by a connective tissue capsule, and inside the organ the capsule extends to form trabeculae. Reticular tissue composed of reticular cells and reticular fibers form a supporting reticular meshwork inside the node. This meshwork **contains two populations of cells**:

- reticular cells which synthesize and secrete reticular fibers and ground substance;
- follicular dendritic cells with filiform processes which are cells of the immune system. They assist in B cell maturation by the presentation of intact antigen to the B cells.

The lymph node contains:

- outer cortex,
- deep (inner) cortex (paracortex), and
- medulla.

Outer cortex is formed by lymphoid tissue whose meshwork is populated by B-cells and macrophages. Within the cortical lymphoid tissue are spherical structures called lymphatic nodules (follicles). Nodules are temporary structures, which may appear and disappear in the same site. Nodules are spherical structures (0,2-1 mm diameter) lacking a connective tissue capsule. They are mainly composed of dense aggregates of B-lymphocytes. When a nodule is unstimulated, it is termed a primary nodule, when active immune responses are underway, it becomes a secondary nodule. **Secondary lymphatic nodule** (fig.64) **consists of**:

- **germinal centre** is central less-stained area, the site of B-lymphocyte proliferation under the antigen influence; contains large proliferating Blymphocytes and plasma cells interspersed with macrophages and dendritic cells.

- **corona** (mantle zone) is more intensely stained peripheral area, Paracortex (situated between the cortex and the medulla) lacks distinct morphological boundaries, is a region occupied by T- lymphocytes. This region has been shown to be thymus-dependent and if the thymus is removed experimentally, the paracortical zone disappears.

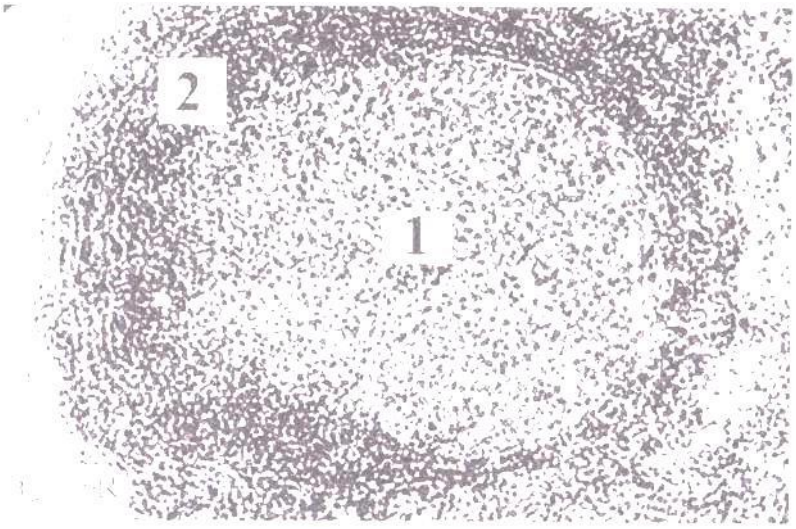


Figure 64. Photomicrograph of lymphatic nodule of lymph node. 1 - germinal center, 2 - corona

Medulla is formed from branching medullary cords of B- lymphocytes, between which the medullary sinuses are found. Lymph circulation The sinuses (fig.70) of the node are irregular spaces formed by reticular tissue containing various lymphocytes, antigen-presenting cells, macrophages. The sinuses act as mechanical filters in which lymph flow is extremely slow and are the sites where many cells are trapped. which contains small resting B cells and dendritic cells.

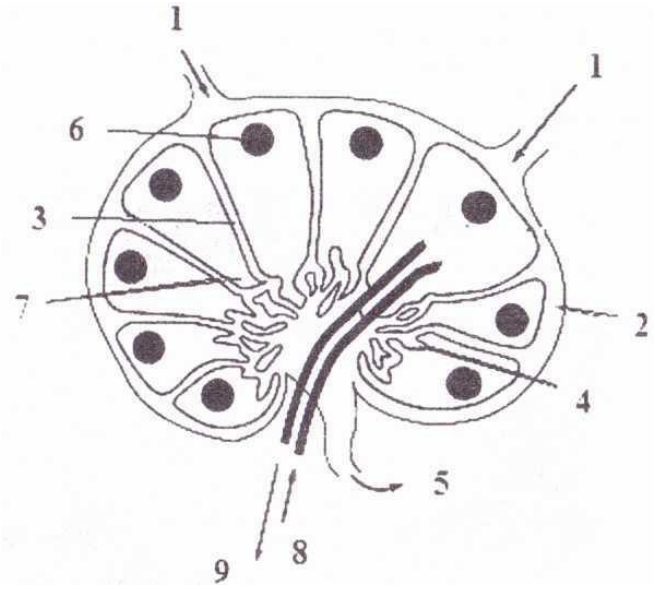


Figure 65. Schematic diagram of lymph node sinuses. 1 - afferent lymphatic vessels, 2 - subcapsular sinus, 3 - intermediate sinus, 4 - medullary sinuses, 5 - efferent lymph vessel. 6 - lymphatic nodule, 7 - medulla, 8 - artery, 9 — vein.

Lymph enters the subcapsular sinus from multiple afferent lymph vessels. The subcapsular sinus communicates through intermediate (peritrabecular) sinuses (run parallel to the trabeculae of the capsule into the inferior of the node) with the medullary sinuses. l.yniph passes through the medullary sinuses and leaves the lymph node at the hilus via a single efferent lymph vessel. Valves in the vessels control the flow.

Spleen .The spleen is a large lymphoid organ situated in the left upper part of the abdomen. The spleen functions in both the immune and hematopoietic systems.
The functions of the spleen as organ of immune system:
1. Removal of macromolecular antigens from the blood.
2. Antigen presentation by antigen presenting cells and initiation of immune response.
3. Antigen-dependent proliferation and differentiation of T- and B-lymphocytes, which ensure the immunological responses.
The functions of the spleen as hematopoietic organ:
1. Removal and destruction of aged, damaged and abnormal erythrocytes and platelets.
2. Retrieval ofiron from erythrocyte hemoglobin.
3. Storage of blood.
4. Formation of the erythrocytes during the fetal life.
Structure of the spleen The spleen (fig.66) is surrounded by a capsule of dense connective tissue that sends trabeculae, which divide the **parenchyma**, or **splenic pulp, into incomplete compartment**s. The medial surface of the spleen has a hilura, which is the site for entry and exit of the blood vessels and nerves.

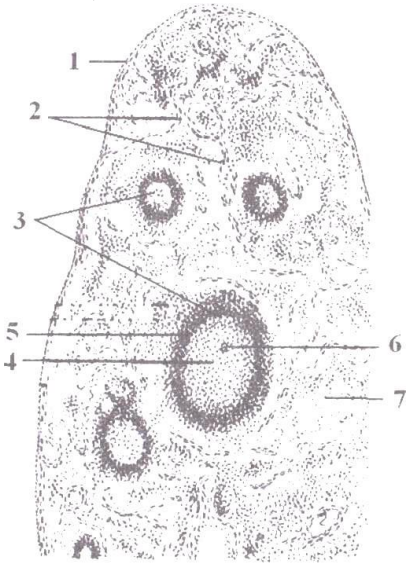


Figure 66. Schematic diagram of the spleen. 1 - capsule, 2 - trabeculae, 3 — white pulp (splenic nodules), 4 - germinal center, 5 - germinal center, 6 - central artery, 7 — red pulp
Stroma of the spleen is formed by reticular tissue consisting of reticular cells and reticular fibers.

The **splenic pulp** is divided into two functionally and morphologically different regions: **white pulp and red pulp**. Between white pulp and red pulp there is the marginal zone.

White pulp. The white pulp (20% of the total mass of the spleen) is composed of lymphoid tissue surrounding an artery. **White pulp consists of**:

- periarterial lymphatic sheaths (PALS);
- lymphatic nodules.

Branches of the splenic artery course through the capsule and trabeculae of the spleen and enter the white pulp. Within the white pulp, these vessels are called the central arteries (fig.67).

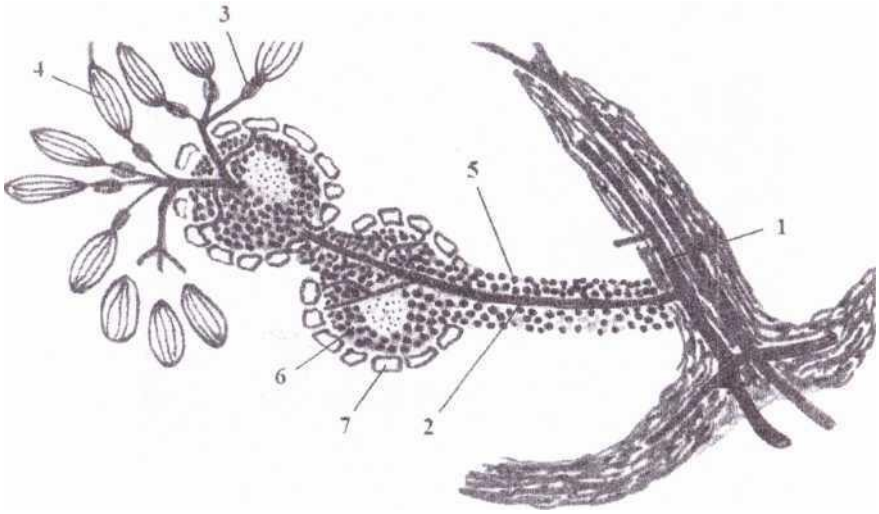


Figure 67. Schematic diagram of the white pulp. 1 - trabecular artery, 2 — central artery, 3 - sheathed capillaries, 4 - splenic sinus, 5 - periarterial lymphoid sheathe (PALS), 6 - splenic nodule, 7 - marginal zone

Lymphoid tissue that surrounds the central artery constitutes the periarterial **lymphatic sheaths** (PALS). The PALS has a cylindrical configuration that conforms to the course of the central artery. Within PALS, there are circumferential layers of reticular cells and reticular fibers that support lymphocytes which are predominantly T-cells. Lymphatic nodules are on periphery of periarterial lymphoid sheaths, are circular masses of lymphoid tissue, and are populated by mainly B-lymphocytes. **Lymphatic nodules displace the central artery, so that is occupies an eccentric rather than a central position. The nodule (fig.73) consists of:**

- **germinal center**, which is central less-stained area, the site of B-lymphocyte proliferation under the antigen influence; Germinal centers develop within 24 hours after antigen influence and may become very large and visible with the naked eye. These enlarged nodules are called splenic nodules or Malpighian corpuscles
- **mantle zone** .The marginal zone is the transition between the white and red pulp. It consists of many sinuses and loose lymphoid tissue. The marginal zone contains few lymphocytes but many active macrophages. It removes

antibodies and Tand B-lymphocytes from the blood and plays a major role in the immunological activity of the spleen.

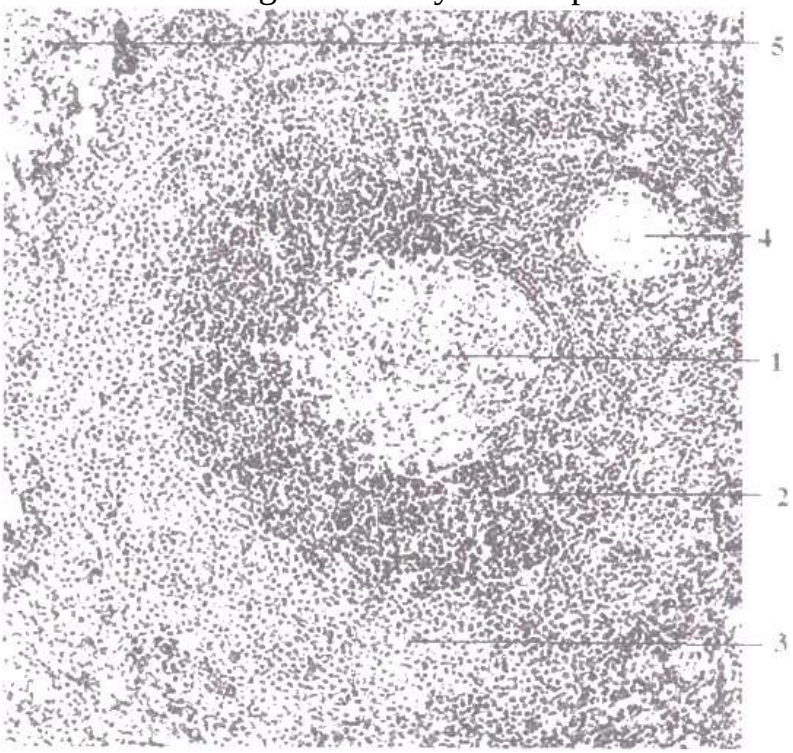


Figure 68. Photomicrograph of splenic nodule. 1 - germinal center, 2 — mantle zone 3 - marginal zone, 4 - central artery, 5 - red pulp.

Red pulp. The red pulp (fig.73) is reticular tissue of diffuse type, which consists of:

- splenic (venous) sinuses separated by
- splenic cords (cords of Billroth). rona) is a narrow zone of small lymphocytes.

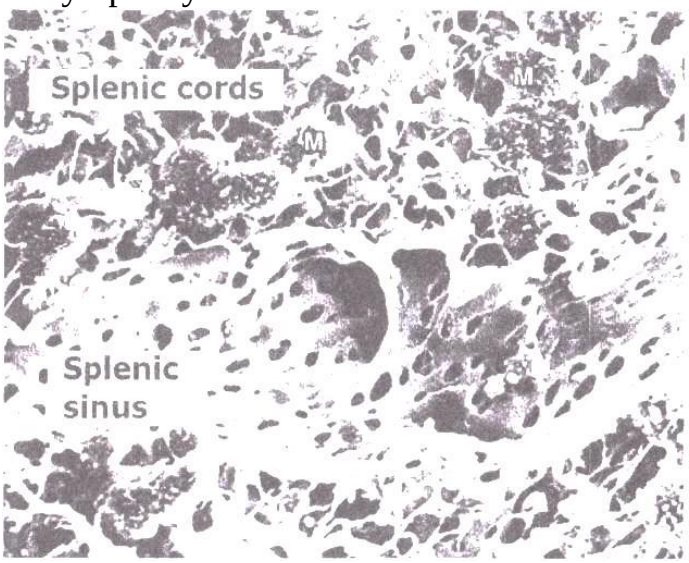


Figure 69. Electron micrograph of red pulp oi the spleen.

Splenic cords consist of loose meshwork of reticular cells and reticular fibers that contains formed elements of the blood (erythrocytes, platelets, and granulocytes),

macrophages, lymphocytes, plasma ceils. **Splenic (venous) sinuses** (fig.74) are long vascular channels with an unusual endothelium and basal lamina.

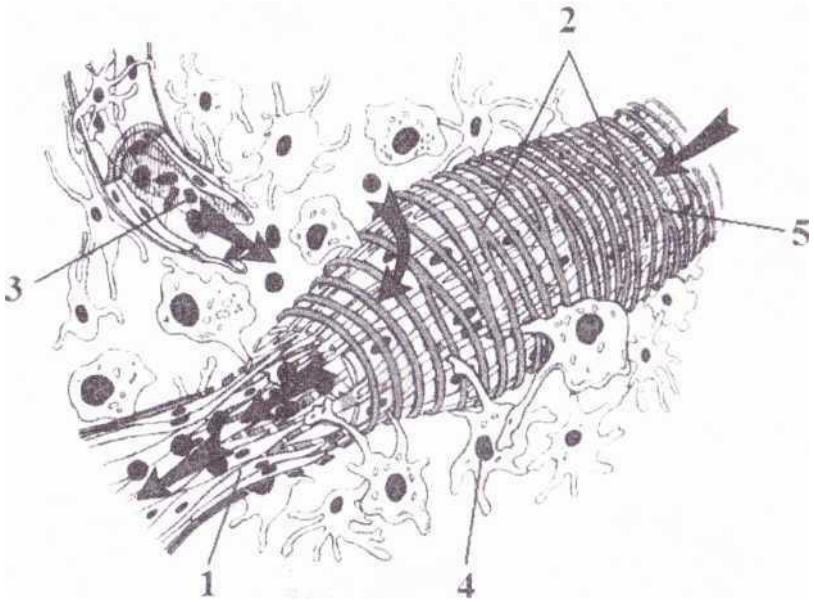


Figure 70. Schematic diagram of splenic sinus. 1 - endothelial cells of splenic sinus, 2 - reticular fibers, 3 - terminal arterial capillaries (open circulation), 4 - phagocytic cells, 5 - closed circulation

The **endothelial cells** are elongated with tapered ends. They lie parallel to the long axis of vessel and have nuclei that bulge into the lumen. The blood cells passing into these vessels from the cords must cross the sinus walls through thin slits between endothelial cells. The basal lamina of the splenic sinuses is fenestrated. Strands of basal lamina loop around the staves of a barrel. These strands are at right angles to the long axes of the endothelial cells. Reticular fibers appear to merge with the perisinusoidal loops of basal lamina. From the sinuses, the blood passes to pulp veins, and finally to trabecular veins.

Spleen blood supply (fig.71)

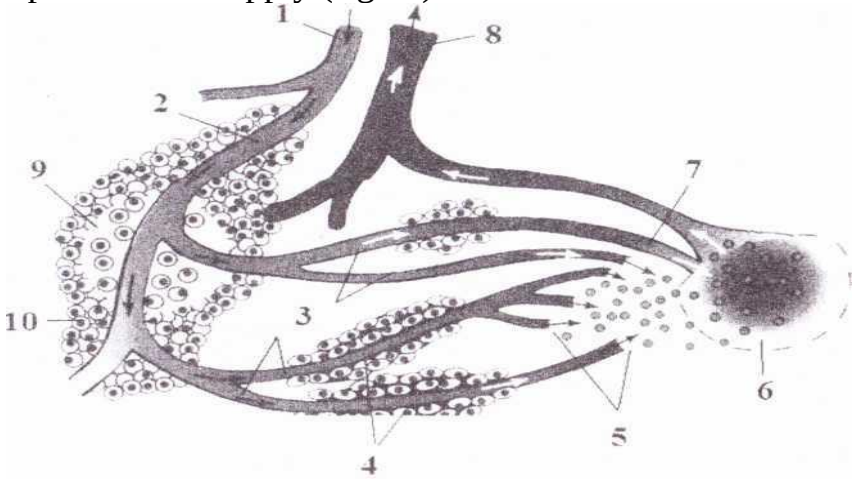


Figure 71. Schematic diagram of spleen blood supply. 1 - trabecular artery, 2 - central artery, 3 - penicillar arteries, 4 - sheathed capillaries, 5 — terminal arterial capillaries (open circulation), 6 — splenic sinus, 7 - closed circulation, 8 - trabecular vein, 9 - splenic nodule, 10 - PALS

The **splenic artery** enters the hilus and branch into trabecular arteries. They enter the parenchyma, are enveloped by lymphatic sheath and are called central arteries. These arteries are surrounded by a sheath of T-lymphocytes (**periarterial lymphatic sheath)**. The central arteries penetrate the lymphatic nodules, usually in the periphery.

After leaving the **white pulp**, the central arteries continue into the red pulp and subdivide to form the penicillar arterioles. The **penicillar arterioles** than continue as arterial capillaries. Some arterial capillaries are surrounded by **ellipsoids** of reticular cells, lymphocytes and macrophages and are thus called sheathed capillaries.

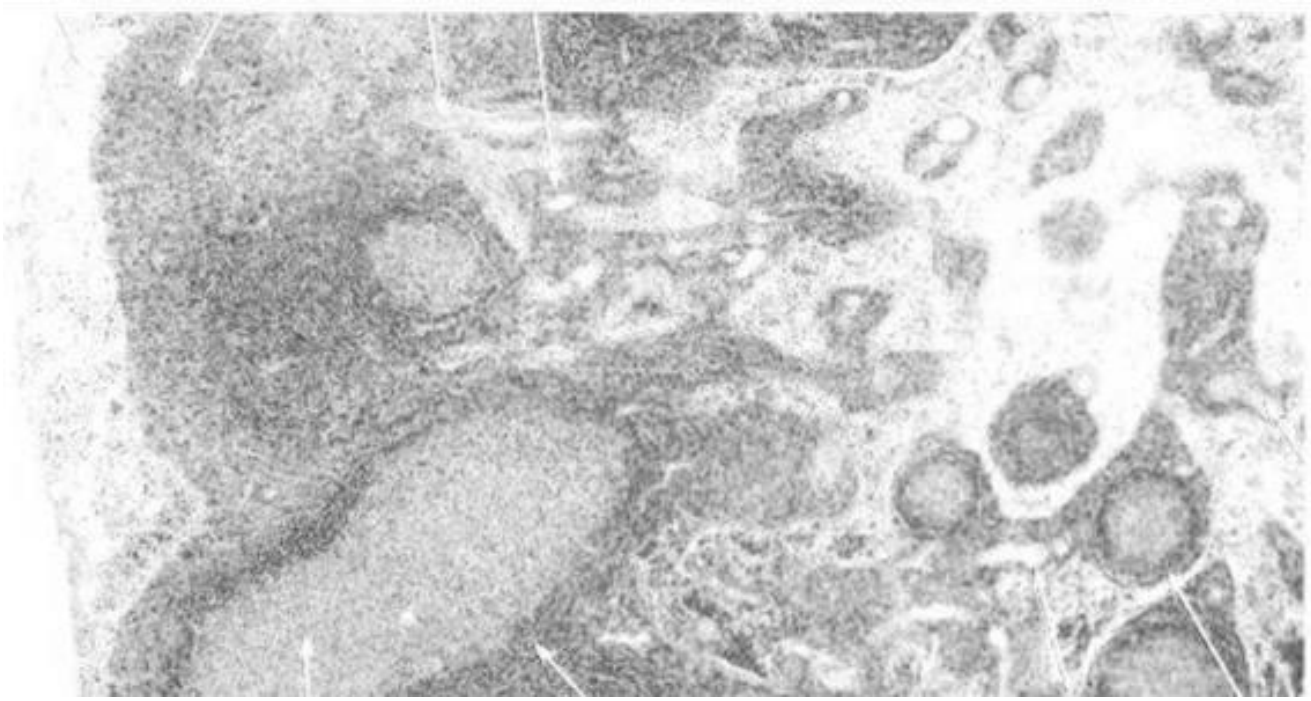
From these vessels blood flows:

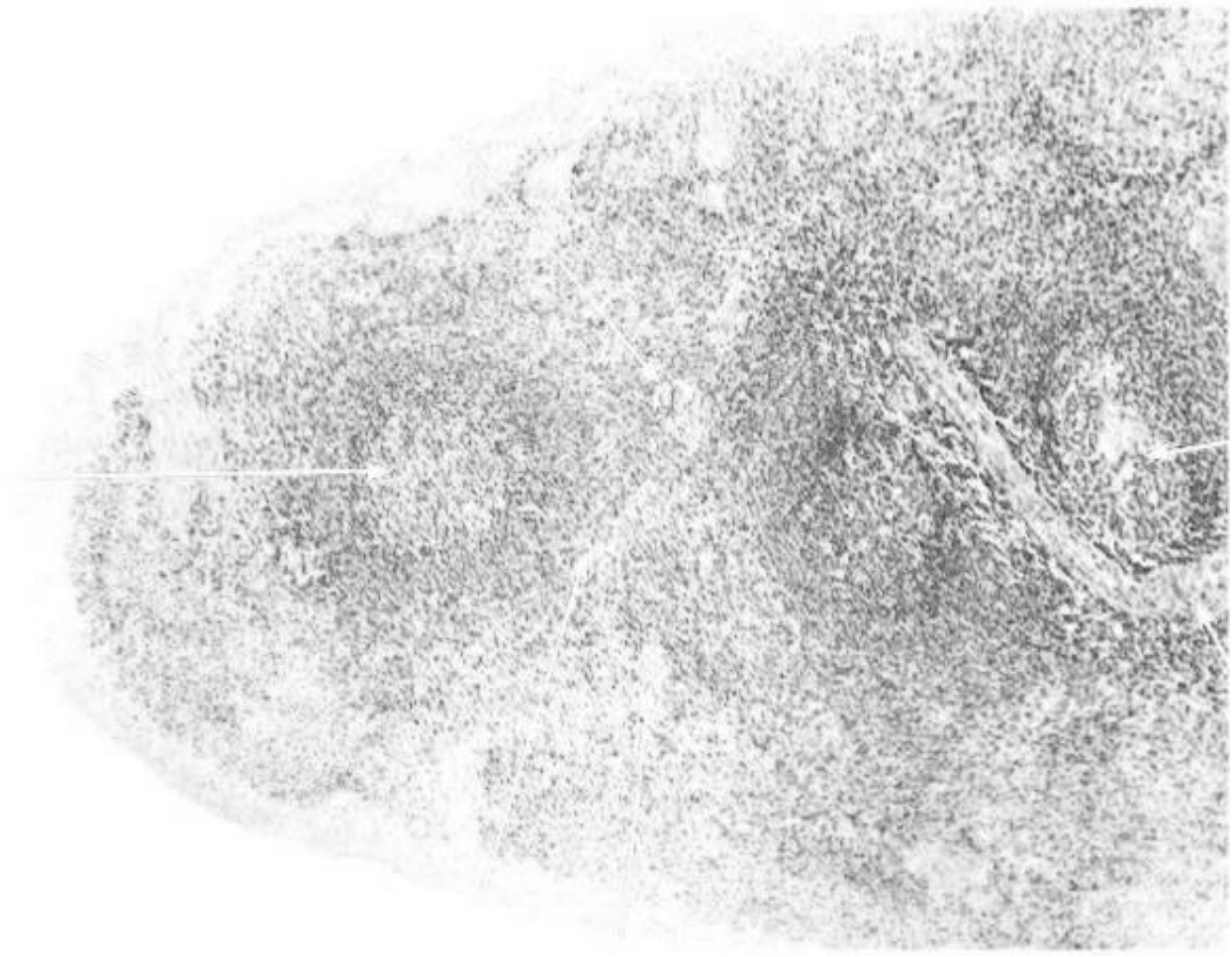
- into the splenic sinuses (**closed circulation**),
- into the splenic cords (**open circulation**), from where blood filters into sinuses. Sinuses empty into the pulp veins.

Practical lessons

1. Spleen: structure and function.
2. Lymph and hemolymph nodes: structure and function.

Paint and mark basic histological structure





Signature of teacher_____

IMMUNE SYSTEM. CELLULAR INTERACTION AT IMMUNE RESPONSES

Overview of the immune system The immune system consists of groups of cells, diffuse lymphoid tissue, and organs that monitor body surfaces and internal fluid compartments and react to the presence of potentially harmful substances and microorganisms. The organs of immune system:

- central or primary (red bone marrow, thymus) and
- peripheral or secondary (spleen, lymphoid nodes, tonsils, appendix, solitary nodules, and Peyer's patches of the ileum).

The cells of immune system have the ability to distinguish "self' (molecules normally present within an organism) from "nonself (foreign substances, i.e., those not normally present) and to coordinate the destruction or inactivation of foreign substances. **The cells of immune system include lymphocytes and various**

supporting cells. **Three types of lymphocytes are recognized: T cells, y B cells, y natural killers (NK) cells**. **Supporting cells** include reticular cells, macrophages, follicular dendritic cells, Langerhans cells and epith elioreticular cells. Supporting cells are organized into meshwork.

Antigens.Antigens are the foreign (nonself) to the organism substances that can induce a specific immune response. Antigens can be infection organism (bacteria, viruses, fungi, parasites), foreign cells and tissues, transformed cells (cancerous cells), or soluble substances (e.g., foreign proteins, polysaccharides, nucleoproteins, or toxins).

Characteristic of T lymphocytes (T cells).T cells represent 60-80% of blood lymphocytes. They have a long lifespan and are involved in cell-mediated immunity. The abbreviation T, in T cell, stands for thymus, since this is the principal organ responsible for the T cell's maturation. T cells originate in the bone marrow and migrate to the thymus, where they differentiate into immunocompetent cells. Initially, lymphocytes are genetically programmed to recognize a single antigen out of virtually an infinite number of possible antigens. This process is termed antigen-independent proliferation and differentiation Then immunocompetent cells migrate to the blood, lymph, and special T- regions of peripheral (secondary) lymphoid organs where they undergo antigen-dependent activation and differentiation into effector lymphocytes (cytotoxic cells, helpers, and suppressors) and memory cells. T memory cells react rapidly to the reintroduction of the same antigens.

Characteristic of B lymphocytes (B cells). B- cells are named so because they were first recognized in the bursa of Fabricius in birds. They have variable lifespan and are involved in humoral immunity by production and secretion of circulating antibodies (immunoglobulins). B- cells represent 20-30 % of blood lymphocytes, derive from bursaequivalent organs (red bone marrow and GALT in mammals) where they undergo **antigen-independent proliferation and differentiation**. Then these cells migrate to the blood, lymph, and special B-regions of peripheral (secondary) lymphoid structures where they proliferate and differentiate into the effector lymphocytes (antibody- secreting plasma cells) and memory cells which react very rapidly to reintroduction of the same antigen. This process is called antigen- dependent activation and differentiation.

Characteristic of natural killer (NK) cells NK cells constitute about 5-10% of circulating lymphocytes. NK cells develop from the same precursor cells as T and B cells. These cells genetically are programmed to recognize transformed cells (tumor cells or infected with a virus). Following recognition of antigens,NK cells release proteins (perforins and fragmentins) that open holes in foreign cell membranes, with consequent self-destruction (a process known as apoptosis) or cell lysis.

Characteristics of human immunoglobulins .Antibodies (immunoglobulins) are circulating plasma glycoproteins that interact specifically with the antigens that elicited their formation. Antibodies are secreted by plasma cells that arise by proliferation and differentiation of B-lymphocytes. Five classes of

immunoglobulins are recognized in humans: IgG, IgA, IgM, FgE and IgD, IgG, the most abundant class, constitutes 85% of serum immunoglobulins.

IgG is principal ig in secondary immune response; stimulates chemotaxis; activates complement; crosses the placental barrier, protects the newborn against infection (passive immunity).

IgA (5-15% in the blood), presents in body secretions (tears, colostrum, saliva, nasal, bronchial, intestinal and prostatic secretions, and the vaginal fluid); is resistant to several enzymes, and protects against the proliferation of microorganisms in body secretions.

IgM (5-10% of serum immunoglobulins) is produced during primary immune response; activates macrophages; is found on the surfaces of Blymphocytes as antigen receptor.

IgE (< 1%) stimulates mast cells to release histamine, heparin; is responsible for anaphylactic hypersensitivity reactions; levels increase in parasitic infections.

IgD (< 1%) is found on the plasma membranes of B- lymphocytes and is involved in the differentiation of these cells.

Characteristic of the plasma cells.The plasma cells are large lymphocytes. They have basophilic cytoplasm and an eccentric nucleus with heterochromatin in a characteristic cartwheel or clock face arrangement. Rough endoplasmic reticulum is concentrically located around of a nucleus. Well developed Golgi complex displaces the nucleus to one side of the cell (**perinuclear halo**).

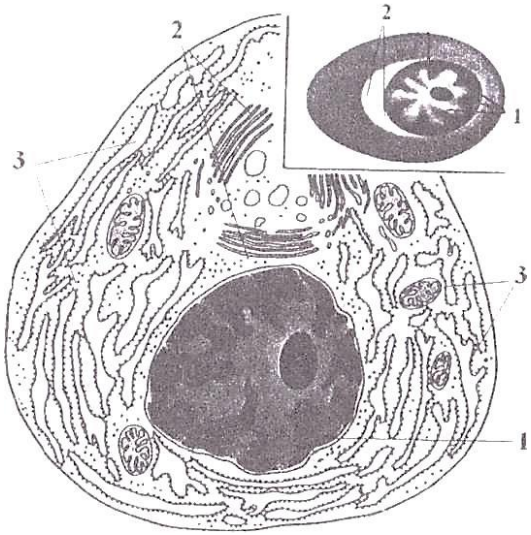


Figure 72. Schcmatic diagram of plasma cell. 1 - chromatin, 2 - Golgi complex (perinuclear halo), 3 - rER

Immune responses to antigens. The initial reaction of the organism to invasion by the antigen is the nonspecific defence (inflammatory response). The inflammatory response may either sequester the antigen with enzymes secreted by neutrophils, or phagocytise the antigen by macrophages. Degradation of the antigen may lead to presentation of portion of the antigen to immunocompetent lymphocytes to elicit the specific immune response. The specific immune response is generated when immunocompetent lymphocytes encounter the antigen. Primary immune response is observed at the first encounter with the antigen. In this case antibodies or specific lymphocytes directed against this antigen can be detected in

the blood in several days. Then a few antigen-specific B cells remain as memory cells, which react very rapidly to reintroduction of the same antigen (secondary immune response).

Basic types of specific immune responses:

1**. Cell-mediated immunity** is mediated by specific cytotoxic T lymphocytes that destroy microorganisms (fungal, mycobacterial), foreign cells (from tumors and transplants), and virus-infected ceils.

2. **Humoral immunity** is related to the presence of circulating antibodies that inactivate or destroy foreign substances. The antibodies are produced by plasma cells derived from B-lymphocytes. Major histocompatibility complex The major histocompatibility complex (MHC) is a large genomic region found on the cel! surface in most vertebrates that encodes MHC molecules. There are two general classes of MHC molecules: class I and class II. Class I MHC molecules are found on almost all cells and present proteins to cytotoxic T cells. Class II MHC molecules are found on certain immune cells themselves, chiefly macrophages and B cells, also known as antigen- presenting cells (APC). These APC ingest microbes, destroy them, and digest them into fragments. The Class II MHC molecules on the APC present the fragments to helper T cells, which stimulate an immune reaction from other cells. Cellular (cell-mediated) immune response Activation phase The cellular immune response begins when antigen, such as virus, enters a body cell. The viral proteins, which are antigens, are broken down by the cell and attached to class 1 MHC proteins . These complexes are presented on the cell's surface.

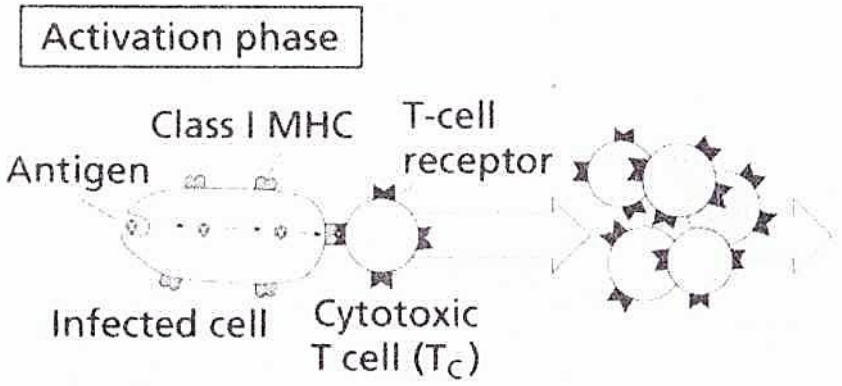


Figure 73. Schematic diagram of the activation phase of cellular immune response.

Cytotoxic T (Tc) cell has T-cell receptors that are specific for the displayed antigen. T-cell receptors bind to the complexes of antigen and class I MHC proteins. This binding activates the Tc cell. They proliferate to form a clone of Tc cell with specific receptors for the same antigen. Effector phase Upon binding, a Tc cell is stimulated to release proteins called perforins. Perforins kill the target cell by poking holes in its plasma membrane and causing the cell to lyse.

Humoral immune response. The humoral immune response is also called the antibody- mediated response because of its use of specific immune-system structures called antibodies. During activation phase macrophage engulfs an antigen by phagocytosis.

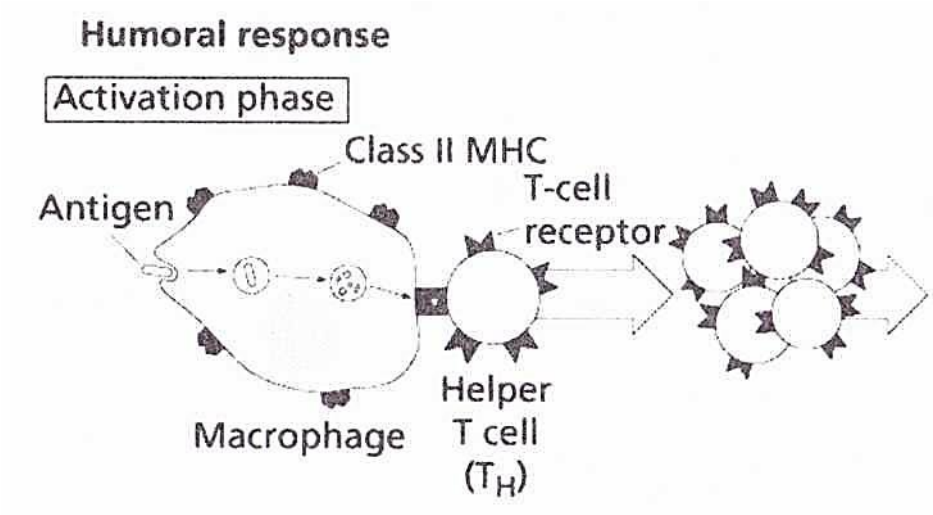


Figure 74. Schematic diagram of the cellular interaction. Activation phase of humoral immune response.

Enzymes of lysosomes of macrophage break down the antigen into fragments (this phenomenon called antigen processing). Within the cell, the processed antigens combine with class II MHC proteins. This complex is displayed on the macrophage's plasma membrane. This display is known as antigen presentation, and macrophage are considered antigen-presenting cell.

Helper T cell (TH cell) has T-cell receptors that can bind to both class II MHC protein and this particular presented antigen. This binding triggers the macrophage to release the cytokine interleukin-1 (IL-1), which activates the THcell The activated THcell now releases its own cytokine interleukin-2 (IL-2), which stimulate the TH cell to proliferate. The cell proliferates to form a clone of TH cells, all with the same T-cell receptors. Next phase, called the effector phase, involves a communication between helper-T cells and B-cells. Activated helper-T cell releases cytokines ("helping signals") that stimulate the B cell to divide. The resulting B-cell develops into either plasma cells or B memory cells.

The plasma cells begin to produce huge quantities of antibodies that can bind and inactivate the antigen. B memory cells retain a "memory" of the specific antigen that can be used to mobilize the immune system faster if the body encounters the antigen later in life. These cells generally persist for years.

HEMOPOIESIS Overview of the hemopoiesis. Mature blood cells have a relatively short life span, and consequently the population must be continuously replaced by the progeny of stem cells produced in the hemopoietic organs. Hemopoiesis is development of the blood cells. Distinguish **embryonic (prenatal) hemopoiesis** which descends in embryonic life and results in development of a blood as tissue, and a **postembryonic (postnatal) hemopoiesis** which represents process of **physiological regeneration of a blood**.

Development of erythrocytes name an erythropoiesis, development of granulocytes - a granulopoiesis, thrombocytes -a thrombopoiesis, development of

monocytes - a monopoiesis, development of lymphocytes and immunocytes - a lympho- and immunopoiesis. At the adult person the hemopoiesis descends in the bone marrow of bone of a skull, ribs, sternum, spondyles, pelvic bones, and epiphyses of the lengthy bones.

In the prenatal period the hemopoiesis serially descends in several developing organs. Prenatal hemopoiesis:

1. Yolk sac **(megaloblastic**) phase: during 2-3 week of development in the wall of the yolk sac the clumps of mesenchymal cells - blood islands - are formed.
2. Cells on periphery of each island form the endothelium of primary blood vessels. The cells of the central part of an island form the first blood cells - primary erythroblasts - the large cells containing a nucleus and embryonic hemoglobin (Hb). Leucocytes and thrombocytes at this stage are not present. On 12-th week the hemopoiesis in a yolk sac comes to an end. Within the second month of development hemopoietic stem cells invade a liver, a lien a thymus and lymph nodes and in these organs different types of blood cells are formed.
3. **Hepatic phase** In a liver the hemopoiesis begins on 5-6 week of development. Granulocytes, thrombocytes and erythrob lasts, and erythrocytes (denuclearized cells) are form here. By the end of 5-th month intensity of a hemopoiesis in the liver decreases.
4. **Splenic phase**.The hemopoiesis in the spleen is most expressed with 4 for 8 month of prenatal development. Here erythrocytes and a small amount of granulocytes and thrombocytes are formed. Directly before of a birth the main function of the spleen the formation of lymphocytes becomes.
5. **Hemopoiesis in the thymus**. On 7-8 week of development in thymus T-lymphocytes are formed. 5. Hemopoiesis in the lymph nodes On 9-10 week of development lymph nodes can produce erythrocytes, granulocytes and megakaryocytes.
6. **Bone marrow phase** .Within 5-th month of development a hemopoiesis begins in the bone marrow where all types of blood cells are formed. By the moment of a birth, after a birth and at the adult the hemopoiesis is limited to the bone marrow and the lymphoid tissue. When the bone marrow is not capable satisfy the increased inquiry about formation of the blood cells, hemopoietic activity of a liver, spleen and lymph nodes can be reduced.

Theory of a hemopoiesis.Now it is proved, that as the common source of development of all formed elements of the blood is pluripotential stem cell This position for the first time is formulated by professor **A.A.Maksimov in the beginning of XX century in the monophyletic (Unitarian) theory** of the hemopoiesis.

Stem cells. Stem cells can produce all blood cell types, because these cells are called pluripotential. Stem cells look like small lymphocytes. Stem cells are

concentrated at the adult person mainly in the red bone marrow, however are found out in the blood, circulating in which they get in other organs of a hemopoiesis. **The basic properties of stem cells**:

- Self-renewal - the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
- Potency - the capacity to differentiate into specialized cell types. Pluripotential stem cells can differentiate into nearly all cells.

Multipotential stem cells can differentiate into a number of cells, but only those of a closely related family of cells. **Oligopotenial stem** cells can differentiate into only a few cells, such as **lymphoid or myeloid stem cells**. **Unipotential cells** can produce only one cell type. The study of stem cells in bone marrow is possible because of experimental techniques that permit analysis of hemopoiesis. In vivo techniques include injecting the bone marrow of normal donor mice into lethaily irradiated mice whose hemopoietic cells have been destroyed. In these animals, the transplanted bone marrow cells develop colonies of hemopoietic cells in the spleen (colony-forming cells - CFC) In vitro investigation of hemopoiesis is made possible through the use of a tissue culture medium made with a layer of cells derived from bone marrow stroma. This medium creates microenvironmental conditions for hemopoiesis. Data from an experiments show that under these suitable microenvironmental conditions, stimulation by growth factors influences the development of the various types of biood cells. Bask compartments of the hemopoietic cells :

I - pluripotential stem cell;
II - multipotential stem cells;
III - uni- or bipotential progenitor cells;
IV - precursor cells (blasts),
V - maturing cells,
VI- mature cells.

Pluripotential stem cell (I) proliferates and forms one cell lineage that will become lymphocytes (lymphoid cells), and another lineage that will form the myeloid cells that develop in bone marrow (granulocytes, monocytes, erythrocytes, and megakaryocytes). Both these types of stem cells are called multipotential stem cells. **The proliferating multipotential stem cells (II)** form daughter cells with reduced potentiality: **uni- or bipotential progenitor cells (III).**Cells forming colonies of specific cell types are called colony-forming cells (CFC), or colony-forming units (CFU). The convention in naming these various cell colonies is to use the initial letter of the cell each colony produces. Thus, MCFC denotes a monocyte-colony-forming cell, CFC-Eo produces eosinophils, and CFC-MG produces monocytes and granulocytes, and so on. **Progenitor cells (III)** have high mitotic activity, self-renewing, common in marrow and lymphoid organs. Uni- or bipotential progenitor cells generate precursor cells (**blasts) (IV). Precursor cells (IV**) have high mitotic activity, not self- renewing, common in marrow and lymphoid organs, unipotential.

From each progenitor cell there is a formation of a concrete kind of cells. The maturing of each kind of cells passes series of stages which in aggregate form compartment of **maturing cells (V).** Mature cells represent last compartment (VI). **All cells of V and VI compartments morphologically can be identified**. **Hemopoietic cytokines**.The differentiation pluripotential cell in unipotential is determined by action of some hemopoietic cytokines, erythropoietin, granulocyte colonystimulating factor, granulocyte-macrophage colony-stimulating factor, monocyte colony-stimulating factor, thrombopoietin, interleukins etc. Cytokines are glycoprotein hormones and stimulating factors that regulate all stages of hemopoiesis. Hemopoietic cytokines are produced by stromal components of hemopoietic tissues and organs. They are produced also by epithelial cells of a thymus, macrophages, T-lymphocytes, cells of an endothelium, and also the cells which were outside of hemopoietic tissues (for example, erythropoietin) is produced by the cells of liver and kidney. 0 **Postnatal hemopoiesis.** In the postnatal period the hemopoiesis is carried out in the special hemopoietic tissues - myeloid and lymphoid. The myeloid tissue is functionally leading tissue of the red bone marrow, which in lumens of tubular and flat bones. **The myeloid tissue contains stem cells and is a place of formation of erythrocytes, granulocytes, monocytes, thrombocytes, B-lymphocytes, precursors of T- lymphocytes and NK-cells (natural killer cells).** The lymphoid tissue is found in lymphoid organs - a thymus, a spleen, lymph nodes, tonsils, Peyer's patches, vermiform appendix and the numerous lymphoid formations available in a wall of organs of various systems. In it there is formation T-and B-lymphocytes, and also plasma cells which provide development of immune responses.

Erythropoiesis .Eryihropoiesis is process of formation and a maturing of the erythrocytes, occurring in myeloid tissue. Erythron is erythroidal differon, representing set of the cells - from stem cells up to mature erythrocytes. BFU - burst forming unit - is named so on the ability to form quickly on semisolid medium colony of erythroidal cells size of some hundreds elements. The first recognizable cell in the erythroid series is the proerythroblast. It is a large cell, its cytoplasm is basophilic. The next stage is represented by the basophilic erythroblast with a strongly basophilic cytoplasm and a condensed nucleus. The **basophilia** of these two cell types is caused by the large number of polyribosomes involved in the synthesis of hemoglobin. During the next stage, **polyribosomes decrease and areas of the cytoplasm begin to be filled with hemoglobin.** Staining at this stage causes several colours to appear in the cell – **the polychromatophilic erythroblast**. In the next step, the nucleus continues to condense and no cytoplasmic basophilia is evident, resulting in a uniformly **acidophilic cytoplasm** - the **orthochromatophilic erythroblast**. This cell puts forth a series of cytoplasmic protrusions and **expels its nucleus, encased in a thin layer of cytoplasm.** The remaining cell still has a small number of polyribosomes that, when treated with the survival dye brilliant cresyl blue, aggregate to form a stained network. This cell is **the reticulocyte**, which soon loses its polyribosomes and becomes a mature red blood cell (**erythrocyte)**.

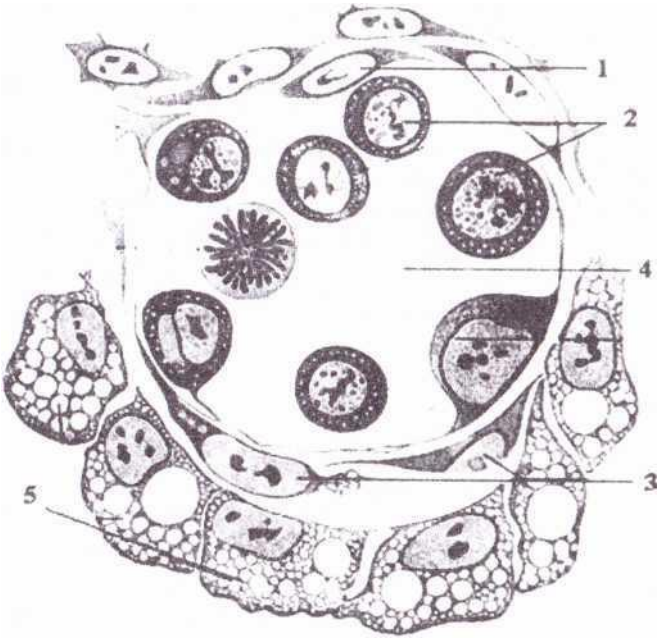


Figure 75. Cross section of the blood island. 1 - endothelium of the wall of blood vessel, 2 - primary blood cells, 3 - mesenchymal cells, 4 - lumen of blood vessel, 5 — eridodermal epithelium

Process of development of erythrocytes is described by sequence: Pluripotential stem cell => multipotential myeloid stem cell (CFU- GEMM) burst forming unit-erythrocyte (BFU-E) => colony forming unit-erythrocyte (CFU-E) => proerythroblast => basophilic erythroblast => polychromatophilic erythroblast orthochromatophilic erythroblast ^ reticulocyte => erythrocyte. Process of a differentiation of precursors of erythrocytes into mature formed elements is accompanied by several gradual changes (fig.76):

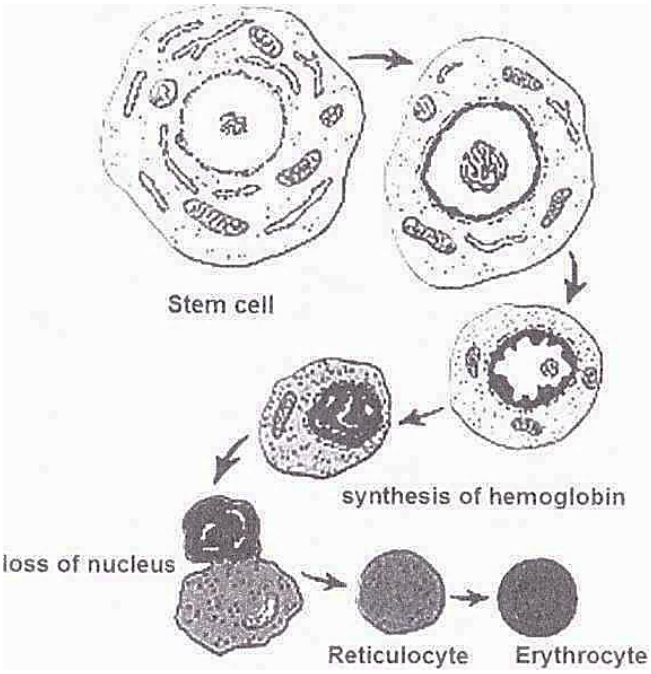


Figure 76. Schematic diagram of erythropoiesis.

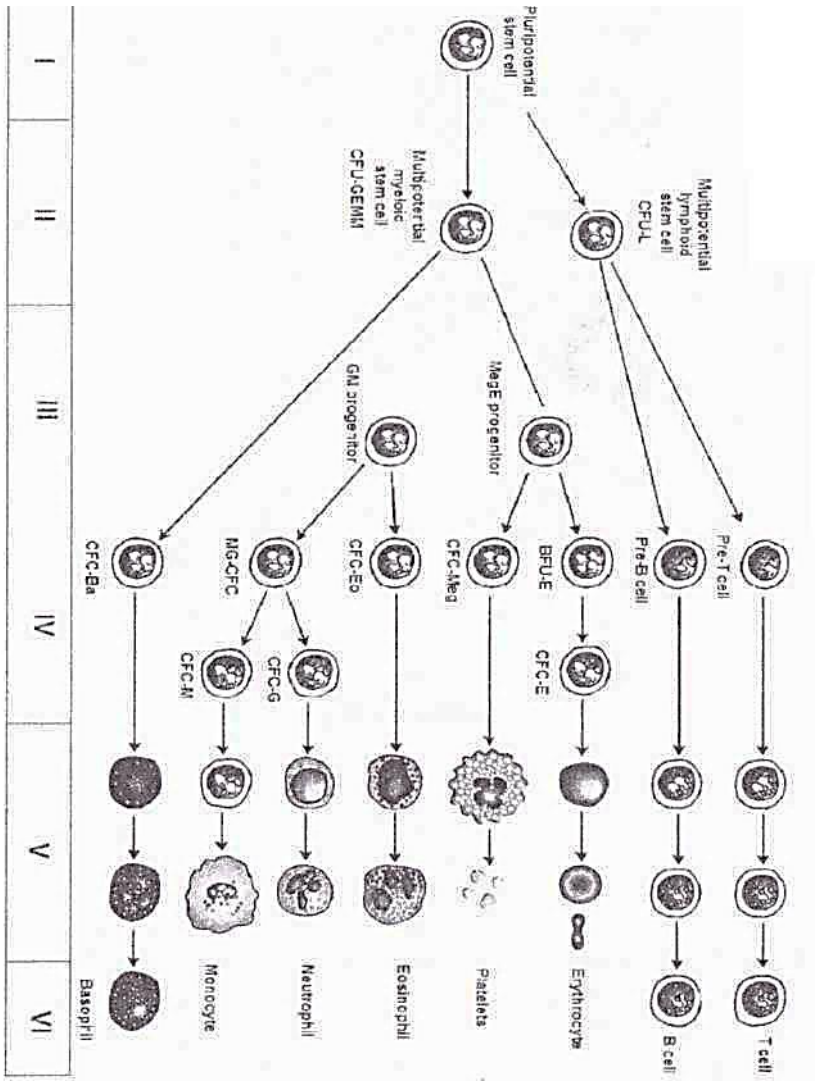


Figure 77. Scheme of hemopoiesis. I-VI- compartments of hemopoietic cells.

- decrease in cell size and loss of cellular organelles,
- decrease of basophilia in cytoplasm due to loss of polysomes,
- increase of acidophilia in cytoplasm due to hemoglobin accumulation,
- decrease in nuclear size and increase in chromatin density (nucleus is eventually extruded),
- loss of ability to divide.

Regulation of erythropoiesis. For erythropoiesis to proceed normally, the red bone marrow must receive adequate supplies of amino acids, iron, and vitamins (including and folic acid) required for protein synthesis. For example, we obtain vitamin B_{12} from dairy products and meat, and its absorption requires the presence of intrinsic factor produced in the stomach. If vitamin $B|_{12}$ is not obtained from the diet, normal stem cell divisions cannot occur and pernicious anemia results. Erythropoiesis is stimulated directly by the peptide hormone erythropoietin and indirectly by several hormones, including thyroxin, androgens, and growth hormone.

Granulopoiesis Granulopoiesis is formation and a differentiation of granulocytes, occurs in the red bone marrow. Process of the differentiation of precursors of

granulocytes into mature cells is accompanied by several gradual changes (similar to erythropoiesis):

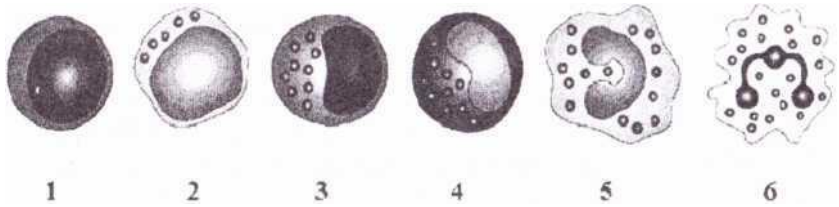


Figure 78. Schematic diagram of granulopoiesis. 1- myeloblast, 2 — promyelocyte, 3 — myelocyte, 4 - metamyelocyte, 5 - band cell, 6 - segmented granulocyte.

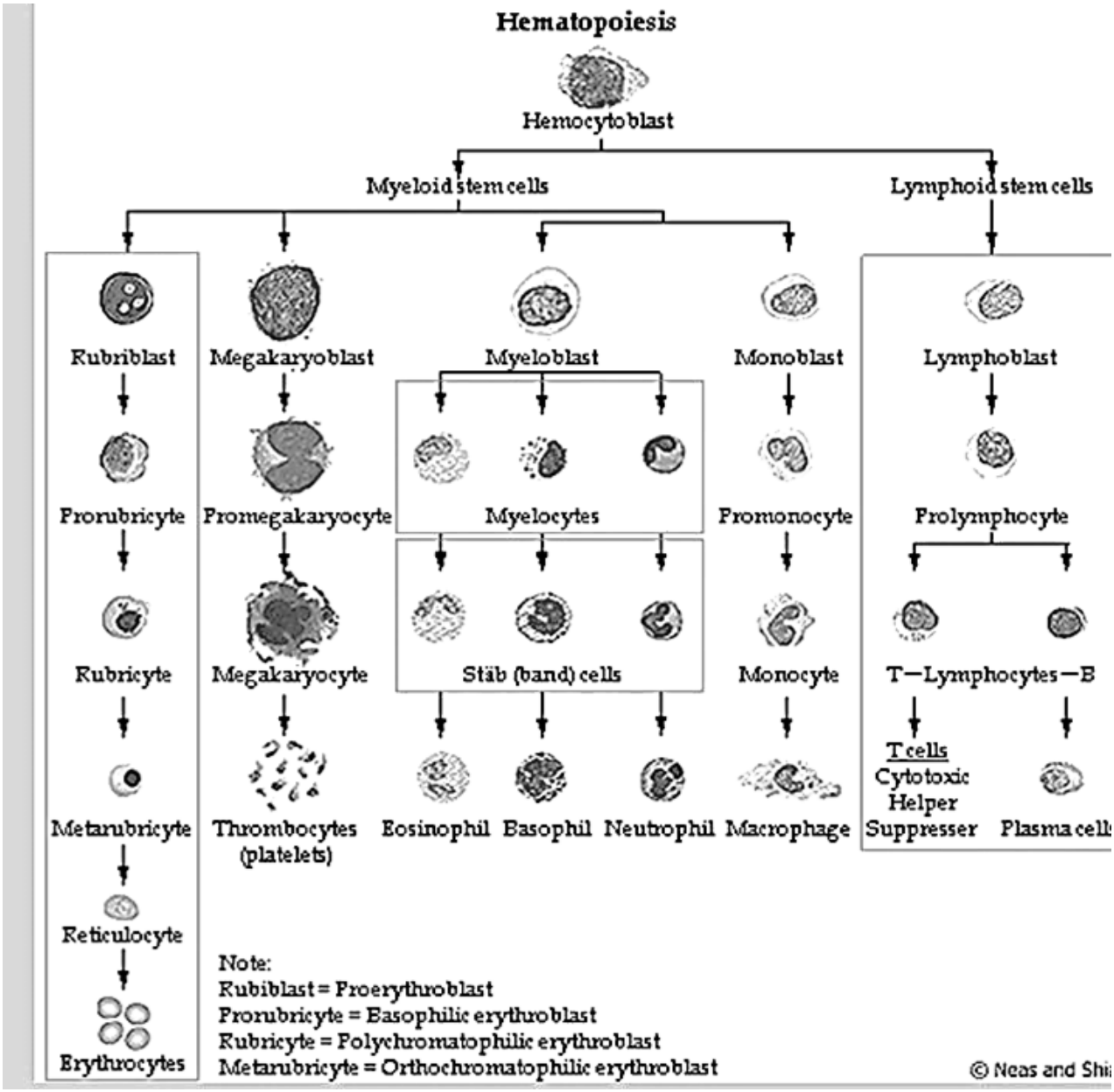
- decrease in cell size,
- change of the shape of a nucleus - from spherical and kidney- shaped to and S- or horseshoe-shaped, its segmentation,
- decrease in amount of azurophilic granules, appearance and increase of specific granules,
- loss of ability to divide.

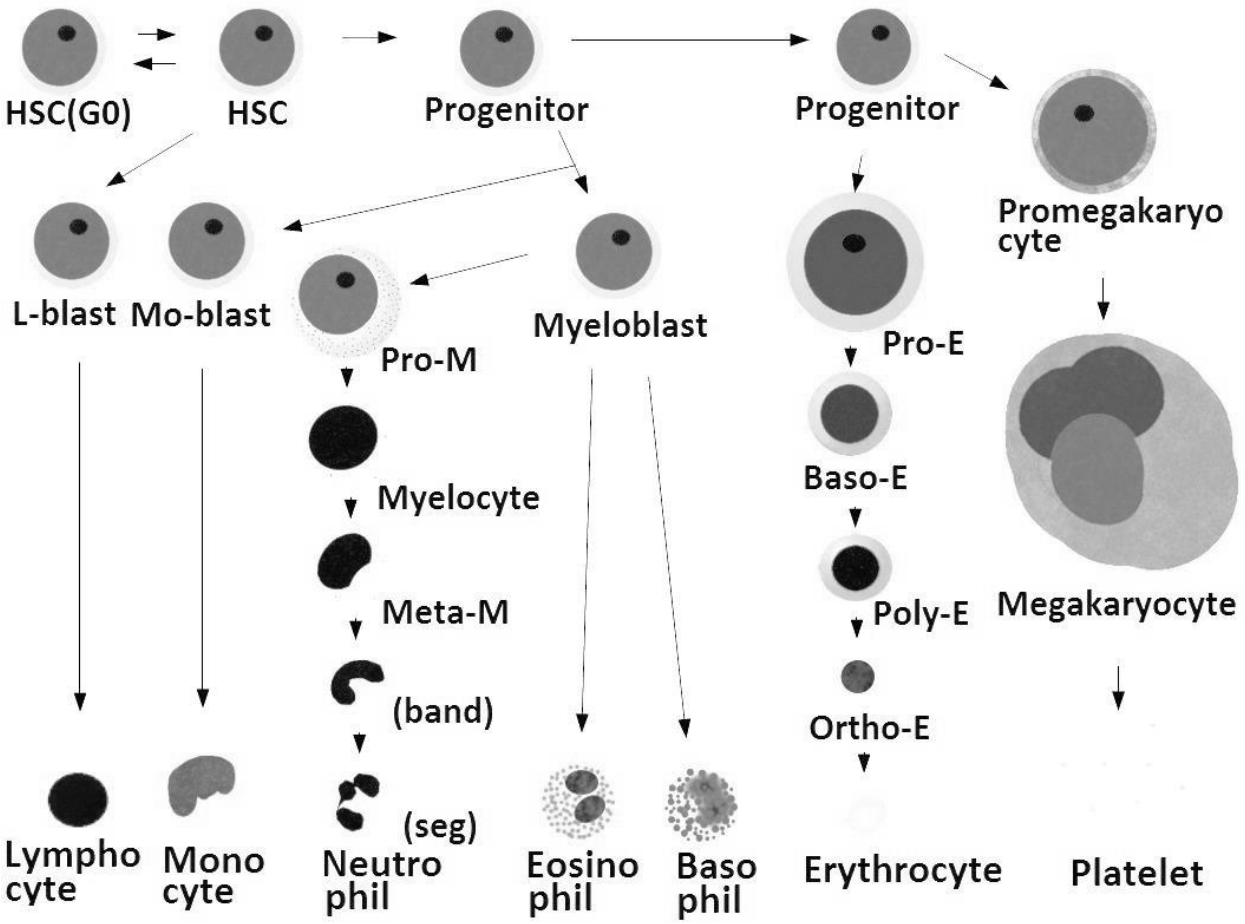
Sequence of the initial stages of development of granulocytes: a) **neutrophilic:** Pluripotential stem cell => multipotential myeloid stem cell (CFJJ- GEMM) => bipotential monocyte-granulocyte-colony-forming cell (MG-CFC) => granulocyte-colony-forming cell (CFC-G); b**) basophilic**: Pluripotential stem cell => multipotential myeloid stem cell (CFU- GEMM) => basophil-colony-forming cell (CFC-Ba); c**) eosinophilic**: Pluripotential stem cell => multipotential myeloid stem cell (CFU- GEMM) => eosinophil-colony-forming cell (CFC-Eo); The subsequent stages of development of granulocytes precede for all three types of cells the same: Myeloblast => promyelocyte => myelocyte => metamyelocyte => band celI => segmented granulocyte.

Monopoiesis is formation and a differentiation of monocytes, occurs in the red bone marrow. Process of development of erythrocytes is described by sequence: Pluripotential stem cell => multipotential myeloid stem cell (CFU- GEMM) bipotential monocyte-granulocyte-colony-forming cell (MG-CFC) => monocytecolony-forming cell (CFC-M) => monoblast => promonocyte => monocyte. Process of transformation of monoblasts into monocytes includes: > increase in the sizes of a cell mainly due to increase of volume of cytoplasm; > decrease of basophilia of cytoplasm; > accumulation in cytoplasm of azurophilic granules; > change of the shape of a nucleus which becomes kidney-shaped.

Thrombopoiesis is formation of platelets in the red bone marrow by fragmentation of the cytoplasm of mature megakaryocytes. Process of development of erythrocytes is described by sequence: Pluripotential stem cell => multipotential myeloid stem cell (CFU- GEMM) => megakaryocyte-colony-forming cell (CFC-Meg) => megakaryoblast => megakaryocyte => platelets. The megakary oblast is 15-50 pm in diameter and has a large ovoid or kidney-shaped

nucleus. The nucleus becomes highly polyploid (it contains up to 30 times as much DNA as a normal cell). The megakaryocyte is a giant cell (35-150 pm in diameter) with an irregularly lobated nucleus. With maturation of the megakaryocyte, numerous invaginations of the plasma membrane ramify throughout the cytoplasm, forming the demarcation membranes. This system defines areas of the megakaryocyte cytoplasm that will be shed as platelets. **Lymphopoiesis** is formation and a differentiation of lymphocytes, occurs in the red bone marrow and lymphoid organs. Process of development of erythrocytes is described by sequence: Pluripotential stem cell => multipotential lymphoid stem cell (CFU- L) => lymphoblast => lymphocytes.





DIGESTIVE SYSTEM

I. ORAL CAVITY AND ASSOCIATED STRUCTURES

Overview of the digestive system Digestive system consists of:

- long muscular alimentary tract (tube) and
- associated glands - salivary glands, pancreas, and liver.

Functions of the digestive system:

1) digestive: a) mechanical and chemical processing of food; b) absorption of nutrients; c) removal of the undigested substances;

2) excretive - removal through a wall of a digestive canal of the harmful substances (at renal insufficiency);

3) immune defence;

4) endocrine - secretion of the hormones having local and system effects.

General plan of structure of the digestive tube. The alimentary tract from the proximal part of the esophagus to the distal part of the anal canal is a hollow tube of varying diameter. This tube has the same basic structural organization throughout its length. The wall of the digestive tube is made up of 4 principal layers:

I.tunica mucosa (mucosa) consists of:

1) lamina epithelialis mucosae consists of only of epithelium;
2) lamina propria mucosae consists of loose connective tissue, rich in blood and lymph vessels, sometimes also contains glands and lymphoid tissue;
3) lamina muscularis mucosae consists of some layers of smooth muscle tissue;

II. tunica submucosa (submucosa) consists of loose connective tissue, contains nerves, blood vessels, and glands in some organs;

III. tunica muscularis (muscularis) consists of some layers of smooth muscle tissue (sometimes of skeletal muscle tissue).

IV. outer layer: **tunica adventitia** consists of loose connective tissue, or **tunica serosa** consists of simple squamous epithelium called mesothelium and small amount of loose connective tissue.

Oral cavity The oral cavity is divided into a vestibule and the oral cavity proper. Features of a structure of a mucosa of an oral cavity

1. epithelium is stratified squamous nonkeratinized or parakeratinized;
2. lamina propria has papillae;
3. muscularis mucosae is absent;
4. submucosa consists of loose connective tissue, contains diffuse small salivary glands.

The oral cavity is lined by a masticatory mucosa, a lining mucosa, and specialized mucosa. The masticatory mucosa is found on the gingival (gums) and the hard palate. It contains stratified squamous keratinized epithelium. The lining mucosa is found on the lips, cheeks, alveolar mucosal surface, floor of the mouth, inferior surfaces of the tongue, and soft palate. The epithelium of the lining mucosa is nonkeratinized stratified squamous. The specialized mucosa is restricted to the dorsal surface of the tongue, where it contains papillae and taste buds.

Practical lessons

1.Digestive tube: general structure, subdivision into portions due to the origin, structure and functions.

2.Oral cavity organs. Peculiarities of mucosa in accordance with functions. Lips, cheeks.

3. Oral cavity organs. Peculiarities of mucosa in accordance with functions. Hard and soft palate, gingiva.

4. Oral cavity organs. Peculiarities of mucosa in accordance with functions. Tongue. Taste buds.

<u>Oral cavity constituents</u>

Lips
Cheeks
Palate
Gingiva (Gums)
Teeth
Tongue
Salivary glands
Tonsils

Lip

Cutaneous (exnernal) aspect

- Stratified squamous keratinized epithelium
- Hair follicles with hair shafts
- Sebaceous glands

Transitional part (vermilion zone)

- Stratified squamous para-keratinized epithelium
- High connective tissue papillae with blood vessels

Mucous (internal) aspect

- Stratified squamous non-keratinized epithelium
- Small labial salivary glands

Cheek

Lining mucosa

Stratified squamous non-keratinized epithelium with prominent connective tissue investment
Buccal salivary glands
Stratum musculare (skeletal muscle)
Zona adiposa
External cutaneous layer

Topographically cheek includes three parts

- Pars maxillaris
- Pars mandibularis
- Pars intermedia

Gingiva (gums)

Gingiva is covered by fully or partially keratinized (parakeratinized) epithelium with high connective tissue papillae
As the epithelium of the gingiva approaches the tooth it attaches to the enamel surface, forming a collar around the neck of the tooth, and is known as junctional epithelium
The 1-2-mm deep space between the gingiva and the tooth is the gingival sulcus.
The gingiva (gum) may be divided into the attached gingiva, which provides a protective covering to the upper alveolar bone, and the free gingiva, which forms a cuff around the enamel at the neck of the tooth. Between the enamel and the free gingiva is a potential space, the ginglval crevice, which extends from the tip of the free gingiva to the cemento-enamel junction.
The thick stratified squamous epithelium, which constitutes the oral aspect of the gingiva, undergoes abrupt transition at the tip of the free gingiva to form a thin layer of epithelial cells tapering to only two or three cells thick at the base of the gingival crevice. This crevicular epithelium is easily breached by pathogenic organisms and the underlying supporting tissue is thus frequently infiltrated by lymphold cells. Collagen fibres of the periodontal membrane radiate from the cementum near the cemento-enamel junction into the dense supporting tissue of the free gingiva, these fibres, together with circular fibres surrounding the neck of the tooth, maintain the role of the gingiva as a protective cuff.

Palate

Septum which separates oral and nasal cavity. It includes 2 components: hard and soft palate.

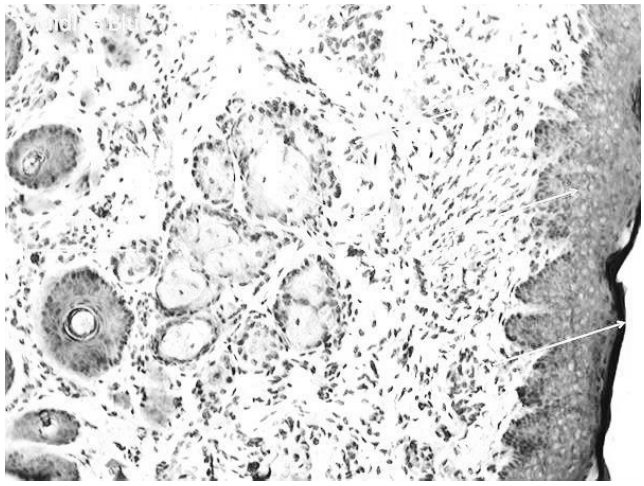
I.Hard palate has 3 zones:

1) adipose,
2) mucous and
3) marginal

At the middle line (epithelial bodies – "perls" may be observed in newborn)

II. Soft palate. Oral surface is lined with stratified squamous nonkeratinized epithelium. **Nasal** surface is cowered by respiratory ciliated epithelium.

Paint and mark basic histological structure



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Tongue The tongue is a muscular organ. It consists of striated muscles covered by mucosa whose structure varies according to the region. The muscle fibers cross one another in 3 planes (fig.80).

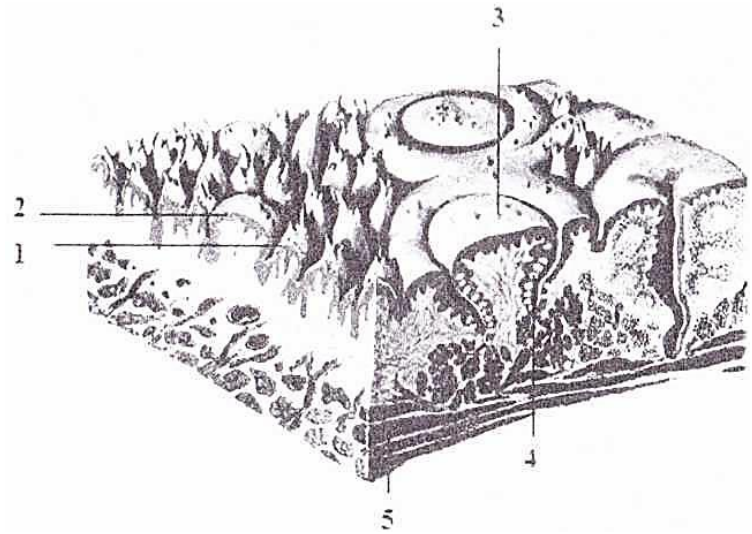


Figure 79. Schematic diagram of a tongue. 1 - filiform papillae, 2 - fungiform papillae, 3 - circumvallate papillae, 4 - taste buds. 5 - striated muscles

Functions of the tongue

1) . The tongue plays an important part in the process of digestion. Due to its muscular nature, tongue can manipulate in any direction, this facilitates the food to be properly mixed with saliva. Tongue can now turn the chewed food into a bolus and push it into the esophagus, from where the food will proceed further into the stomach through the peristaltic movement.

2) . The tongue carries on its surface the taste buds which send information to the brain about the nature of the food being eaten. It seems likely that the sensation of taste is not merely to make eating a pleasure, but also to act as a protective mechanism' designed to cause the rejection of noxious (harmful) foods. 3) .The tongue is responsible for speech.

The **dorsal surface** of the tongue is lined by specialized mucosa, is irregular, because contains a great number of small eminences called papillae.

Mucosa of the dorsal surface consists of 2 layers:

1) stratified squamous parakeratinized epithelium;

2) lamina propria consisting of loose connective tissue, which is strongly adherent to the muscles. Papillae of the tongue are projections of the epithelium and lamina propria.

Distinguish 4 types of the papillae.

1**. Filiform papillae** have elongated conical shape, are most numerous, covered with the stratified squamous highly keratinized epithelium, do not contain taste buds (fig.80).

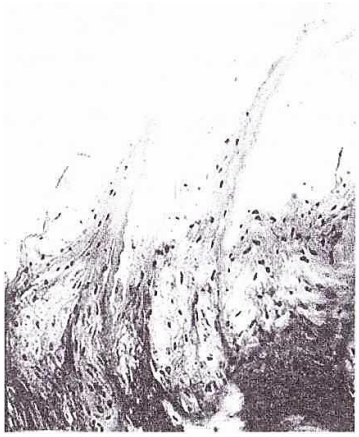


Figure 80.Photomicrograph of the filiform papillae of the tongue

2. **Fungiform papillae** have broad rounded top and a narrow base, are present among the filiform papillae. These papillae have stratified squamous nonkeratinized epithelium and contain taste buds (fig.81).

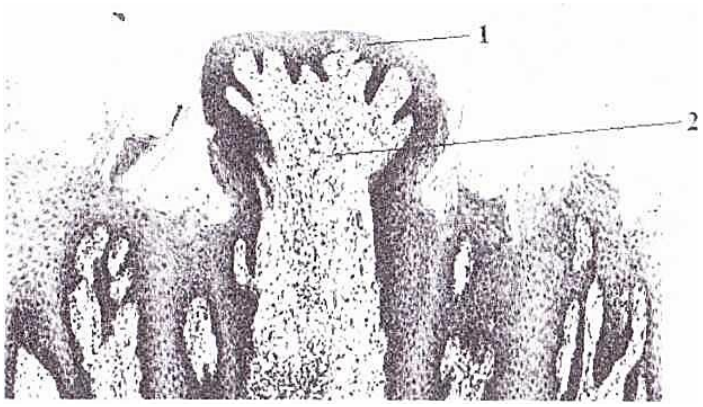


Figure 81. Photomicrograph of the fungform papilla of the tongue. 1 - stratified squamous nonkeratinized epithelium, 2 - connective tissue

3. **Foliate papillae** are poorly developed in humans. They consist of two or more parallel ridges and furrows on the dorsolateral surface of the tongue contain some taste buds (fig.82).

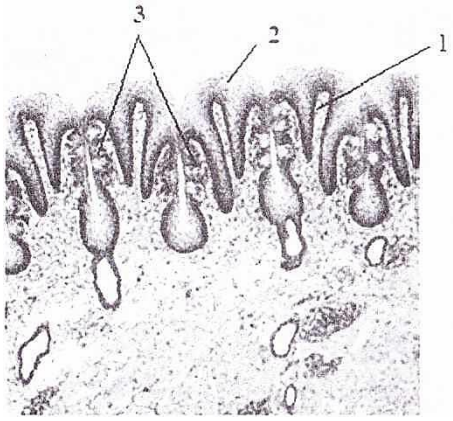


Figure 82. Photomicrograph of the foliate papillae of the tongue. 1 — papilla, 2 - stratified squamous nonkeratinized epithelium, 3 - taste

4. **Circumvallatepapillae** are 6-15 largest papillae, which situated in the V region in the posterior portion of the tongue. Each papilla has a broad rounded top, a narrow base and is surrounded by a circular groove, whose outer wall is called vallum. Taste buds are numerous (fig.83)

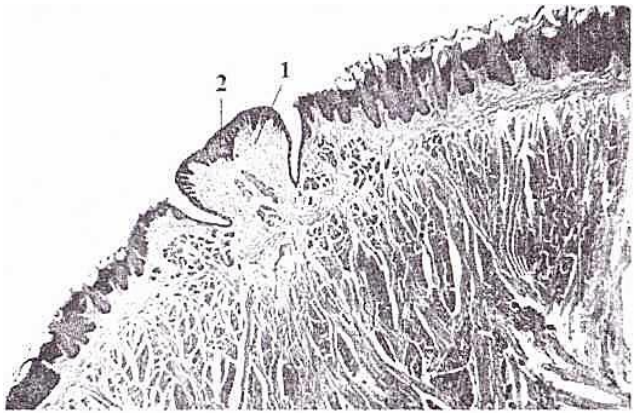


Figure 83. Photomicrograph of the circumvallate papilla of the tongue. I - papilla, 2 - stratified squamous nonkeratinized epithelium

The lower surface of the tongue (fig.84) is lined by lining mucosa. Mucosa is smooth, and consists of 3 Sayers:

1) stratified squamous nonkeratinized epithelium;
2) lamina propria;
3) submucosa.

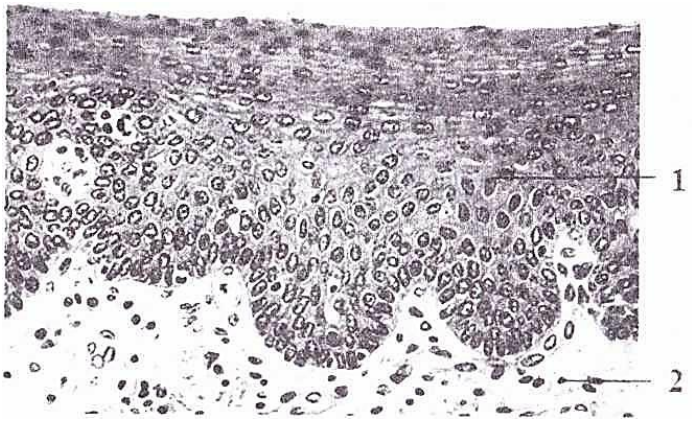
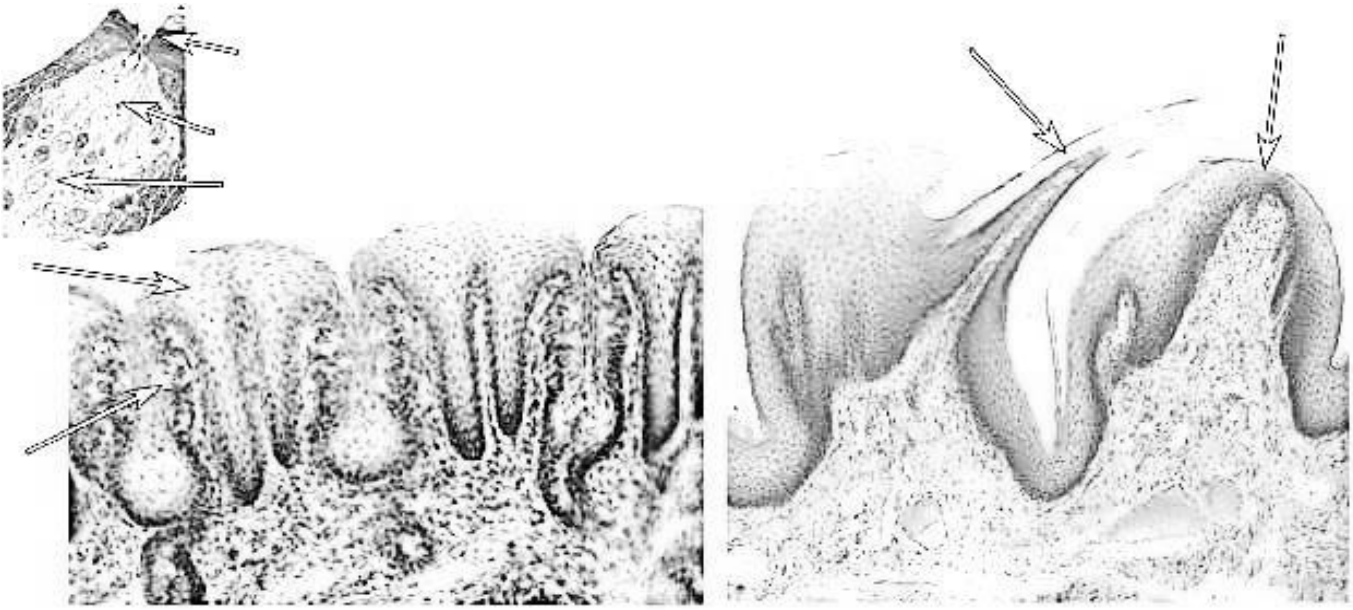


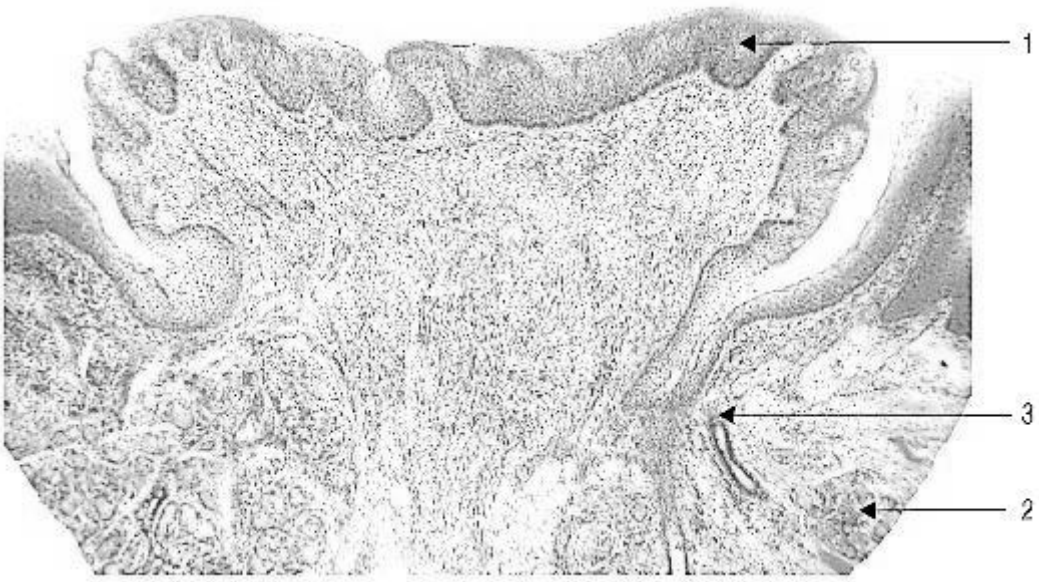
Figure 84. Photomicrograph of the lower surface of the tongue. 1 - stratified squamous nonkeratinized epithelium, 2 - lamina propria

Practical lessons

1.Structure and functions of the dorsal surface of the tongue.
2. Structure and functions of the filiform papillae.
3. Structure and functions of the foliate papillae.
4. Structure and functions of the circumvallatepapillae.

Paint and mark basic histological structure





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Tonsils

The tonsils are organs composed of aggregates of incompletely encapsulated lymphoid tissues that lie in of the initial portion of the digestive tract. The palatine, lingual, pharyngeal and tubal tonsils (adenoids) form Waldeyer's ring.

Palatine tonsil. Two palatine tonsils (fig.86) are located in the lateral walls of the oral part of the pharynx. Their surface is covered by stratified squamous nonkeratinized epithelium which forms deep crypts, and the resulting increase of the surface area is one way to facilitate the contact of antigens with the immune cells. The tonsil contains numerous lymphoid follicles (nodules) with germinal centers.

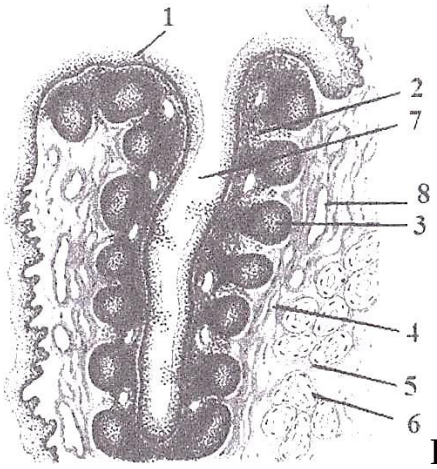


Figure 85.Schematic diagram of the tonsil. 1 - epithelium, 2 - lamina propria, 3 - lymphoid follicle, 4 — smooth muscle cells, 5 — submucosa, 6 — salivary glands, 7 - crypt, 8 - blood vessel.

The base of the tonsil is separated from underlying muscle by a connective tissue hemicapsule. This capsule acts as a barrier against spreading tonsillar infections.

Teeth and Associated structures Each tooth is composed of 3 parts (fig.86):

1) crown is the portion of the tooth that projects above the gingiva (gum);

2) one or more roots are situated below the gingival that hold the teeth in bony sockets called alveoli, one for each tooth;

3) neck is constricted part between crown and root.

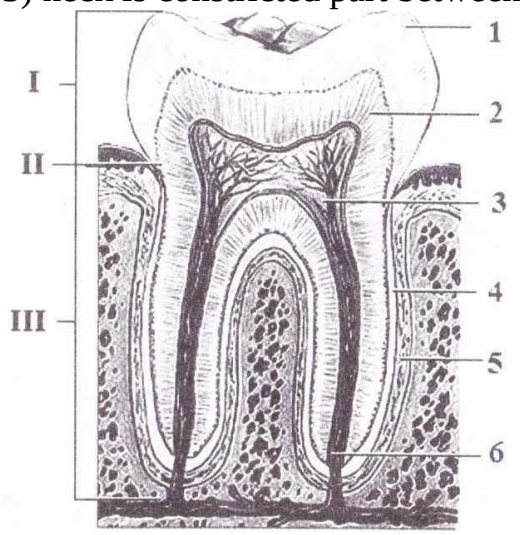


Figure 86. Schematic diagram of tooth. I - crown, II - neck, III - root,] - enamel, 2 - dentin, 3 - pulp, 4 - cementum, 5 - periodontal ligament, 6 - nerve and blood vessels.

Teeth are made up of 3 specialized tissues: dentin, enamel and cementum. Within a tooth there is central pulp cavity occupied by dental pulp.

Dentin The dentin is a calcified tissue of the tooth; it is covered by enamel on the crown and cementum on the root and surrounds the entire pulp.

Dentin is made up of:

70% inorganic materials (hydroxyapatite, which is a crystalline calcium phosphate - Ca,0(PO4)6(OH)2),

20% organic materials (collagen proteins),

10% water.

The organic matrix of dentin is secreted by odontoblasts, cells that line the internal surface of the tooth, separating it from the pulp cavity. Odontoblasts have the structure of protein-secreting cells. These cells have slender, branched cytoplasmic extensions (odontoblast processes) that penetrate perpendicularly through the dentin. Dentin consists of microscopic channels, called dentinal tubules (fig.87), w'hich radiate outw'ard through the dentin from the pulp to the exterior cementum or enamel border. These tubules contain fluid and odontoblast processes.

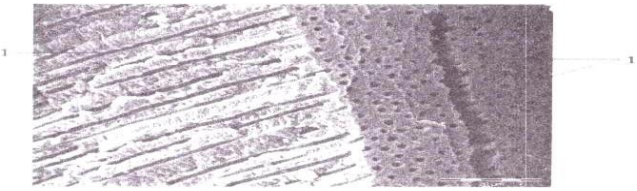


Figure 87. Electron micrograph of dentin. 1 - dentinal tubules

There are three types of dentin.

Primary dentin is the outermost layer of dentin, it borders the enamel.

The outer layer closest to enamel is known as mantle dentin. This layeris unique to the rest of primary dentin. Mantle dentin is formed by newly differentiated odontoblasts. Below it the circumpulpal dentin is situated. This is a more mineralized dentin which makes up most of the dentin layer; it is secreted after the mantle dentin by the odontoblasts.

Secondary dentin (regular secondary dentin) is a layer of dentin produced after the root of the tooth is completely formed. It grows much more slowly than primary dentin. It has a similar structure to primary dentin, although its deposition is not always even around the pulp chamber.

Tertiary dentin (irregular secondary dentin or reparative dentin) is created in response to a stimulus, such as a carious attack. Tertiary dentin is deposited rapidly, with a sparse and irregular tubular pattern and some cellular inclusions known as osteodentin.

Enamel The enamel along with dentin, cementum, and dental pulp is the hardest substance of the human body, the richest in calcium and avascular. It consists of about

95% calcium salts (mainly hydroxyapatite),

1% organic material (collagen proteins),

4% water. The enamel contains (fig.88):

1) elongated enamel rods that are bound together by

2) interrod enamel. Enamel rod is a tightly packed mass of hydroxyapatite crystals in an organized pattern.

Figure 88. Electron micrograph of enamel. 1 - enamel rods, 2 - interrod enamel

Enamel rods are found in rows along the tooth, and within each row, the long axis of the enamel rod is generally perpendicular to the underlying dentin. Both interrod enamel and enamel rods are formed of hydroxyapatite crystals; they differ only in the orientation of the crystals.

Cementum. The cementum is a specialized calcified substance covering the dentin of the neck and root of a tooth, Cementum is similar in composition to bone, although Haversian systems and blood vessels are 370 absent. It is thicker in the apical region of the root, where are cementocytes, cells with appearance of osteocytes. Like osteocytes, cementocytes are encased in lacunae that

communicate through canaliculi. Cementum is secreted by cells called cementoblasts.

The chemical composition of cementum:

65% inorganic material (mainly hydroxyapatite),

23% organic material (mainly collagen typel) and

12% water.

Distinguish two types of cementum:

acellular cementum has no cellular components, covers all surface of the root of the tooth as a thin layer of calcified matrix;

cellular cementum covers 1/3-1/2 of the root apex, contaias cementocytes and calcified matrix. The main role of cementum is to anchor the tooth by attaching it via the periodontal ligaments. It also plays an important role in forming of new teeth. Its bottom surface is tangent to the periodontal ligaments running through the jaw' (via collagen fibers), and the upper portion of the surface is firmly cemented to the dentin of the tooth. Dental pulp The dental pulp is the central part of the tooth filled with soft connective tissue. The central region of the coronal and radicular pulp contains large nerve trunks and blood vessels.

Dental pulp has three layers (from innermost to outermost):

1) cell rich zone contains fibroblasts and undifferentiated mesenchvmal cells;

2) cell free zone (zone of Weil) is rich in both capillaries and nerve networks;

3) odontoblastic layer contains cell bodies of the odontoblasts.

Cells found in the dental pulp include fibroblasts (the principal cells), odontoblasts, macrophages, granulocytes, mast cells and plasma cells. Associated structures The associated structures of the tooth responsible for to attach the tooth to surrounding tissues and to allow sensations of touch and pressure:

cementum;

periodontal ligament;

alveolar bone;

gingiva.

Periodontal ligament is composed of a special type of dense connective tissues whose fibers penetrate the cementum of the root and bind it to the bony wall of its socket. Its fibers are organized so as to support the pressures exerted during mastication.

Alveolar bone forms the sockets and is in immediate contact with the periodontal ligament. It is primary bone in which the collagen fibers are not arranged in lamellar pattern. These fibers are arranged in bundles that penetrate this bone and the cementum. **Gingiva** is a mucous membrane bound to the periosteum of the maxillary and mandibular bones. It is lined by stratified squamous keratinized epithelium. This epithelium is bound to the tooth enamel. Between the enamel and the epithelium is the **gingival crevice** - a small deepening surrounding the crown. 0 Tooth development At about 6 weeks of gestation the oral epithelium proliferates, bulges into the underlying mesenchyme and forms a dental lamina (fig.90).

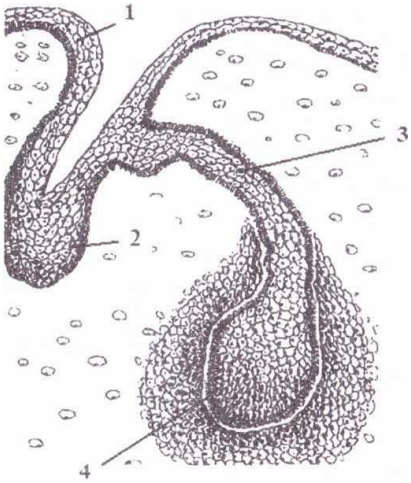


Figure 90. Schematic diagram of developing tooth. 1 - oral epithelium, 2 - vestibular lamina, 3 - dental lamina, 4 - enamel organ

The dental lamina connects the developing tooth bud to the epithelial layer of the mouth for a significant time. Tooth development is divided into the following stages:

bud stage,
cap stage,
bell stage, and finally
maturation (crown stage).

1) **Bud stage.** In each quadrant of the mouth, the dental lamina then develops globular swellings (tooth buds). The tooth bud is the group of cells at the end of the dental lamina.

2) **Cap stage.** Mesenchymal cells aggregate near the pole of tooth bud. These cells are called the dental papilla. At this point, the tooth bud grows around the mesenchymal aggregation, taking on the appearance of a cap, and becomes the enamel (or dental) organ. A condensation of mesenchymal cells called the dental follicle surrounds the enamel organ and limits the dental papilla. Eventually, the enamel organ will produce enamel, the dental papilla will produce dentin and pulp, and the dental follicle will produce all the supporting structures of a tooth.

3)Bell stage.The dental organ is bell-shaped during this stage (fig.91).

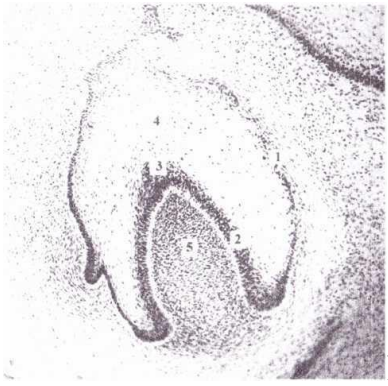


Figure 91. Photomicrograph of developing tooth. 1 - outer enamel epithelium, 2 - inner enamel epithelium. 3 - stratum intermedium, 4 - stellate reticulum, 5 - dental papilla

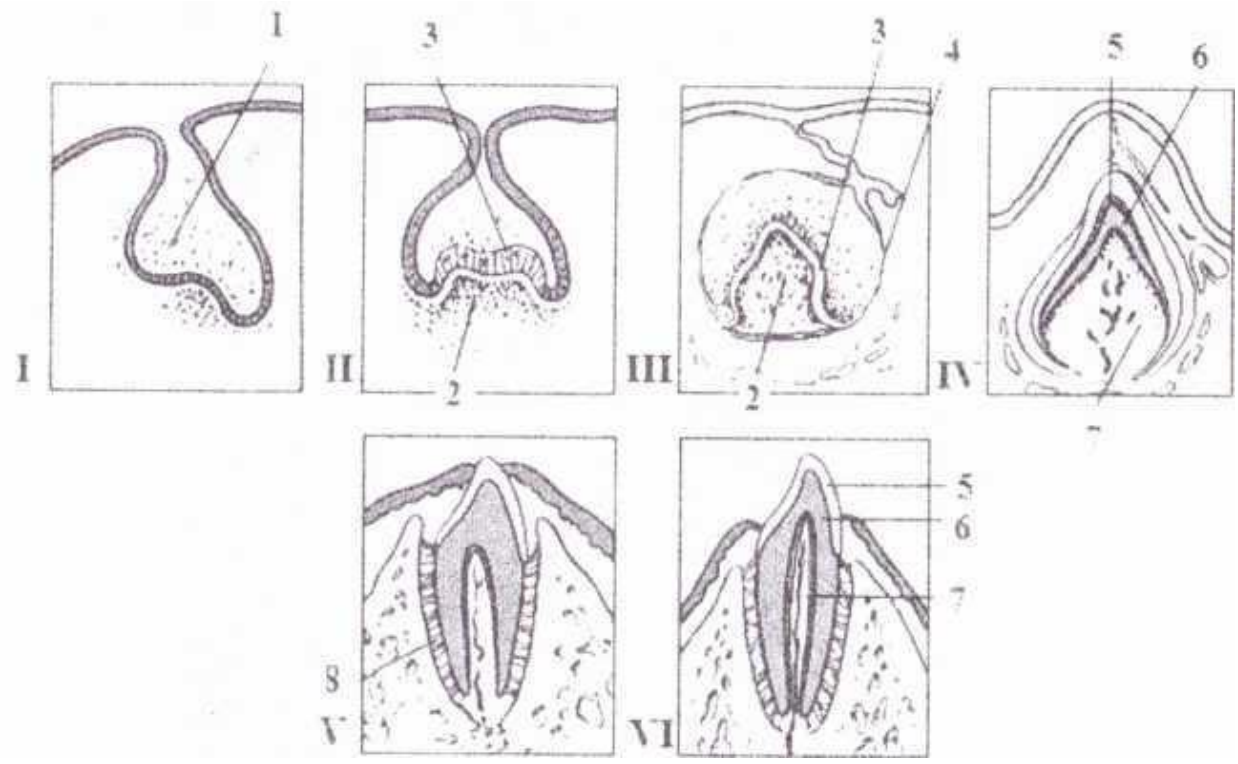
Cells of the enamel organ are divided into three layers.

Cuboidal cells on the periphery of the dental organ are known as outer enamel epithelium.

The columnar cells of the enamel organ adjacent to the dental papilla are known as inner enamel epithelium.

The stellate reticulum is a group of cells located in the center of the enamel organ of a developing tooth.

These cells are star shaped and synthesize glycosaminoglycans. The cells between the inner enamel epithelium and the stellate reticulum form a layer known as the stratum intermedium. The cells of inner enamel epithelium give rise to ameloblasts, which produce enamel. The dental papilla contains cells that develop into odontoblasts, which are dentin-forming cells. Mesenchymal cells within the dental papilla are responsible for formation of tooth pulp (fig.92). The dental follicle gives rise to eementoblasts, osteoblasts, and fibroblasts. Cementoblasts form the cementum of a tooth. Osteoblasts give rise to the alveolar bone around the roots of teeth. Fibroblasts develop the periodontal ligaments which connect teeth to the alveolar bone through cementum.



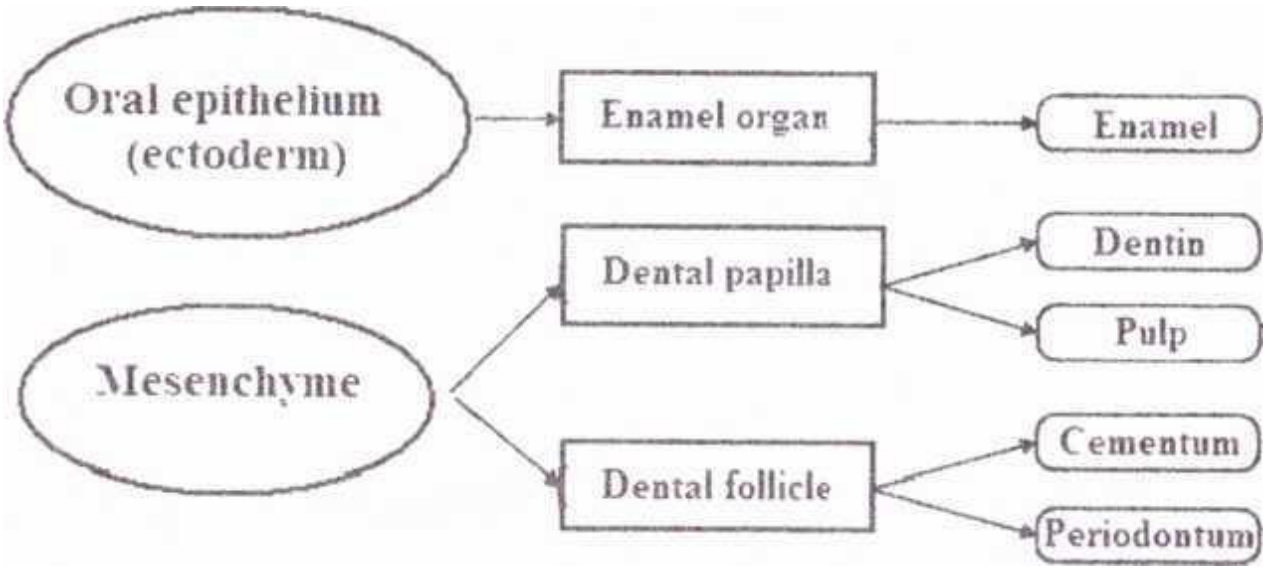


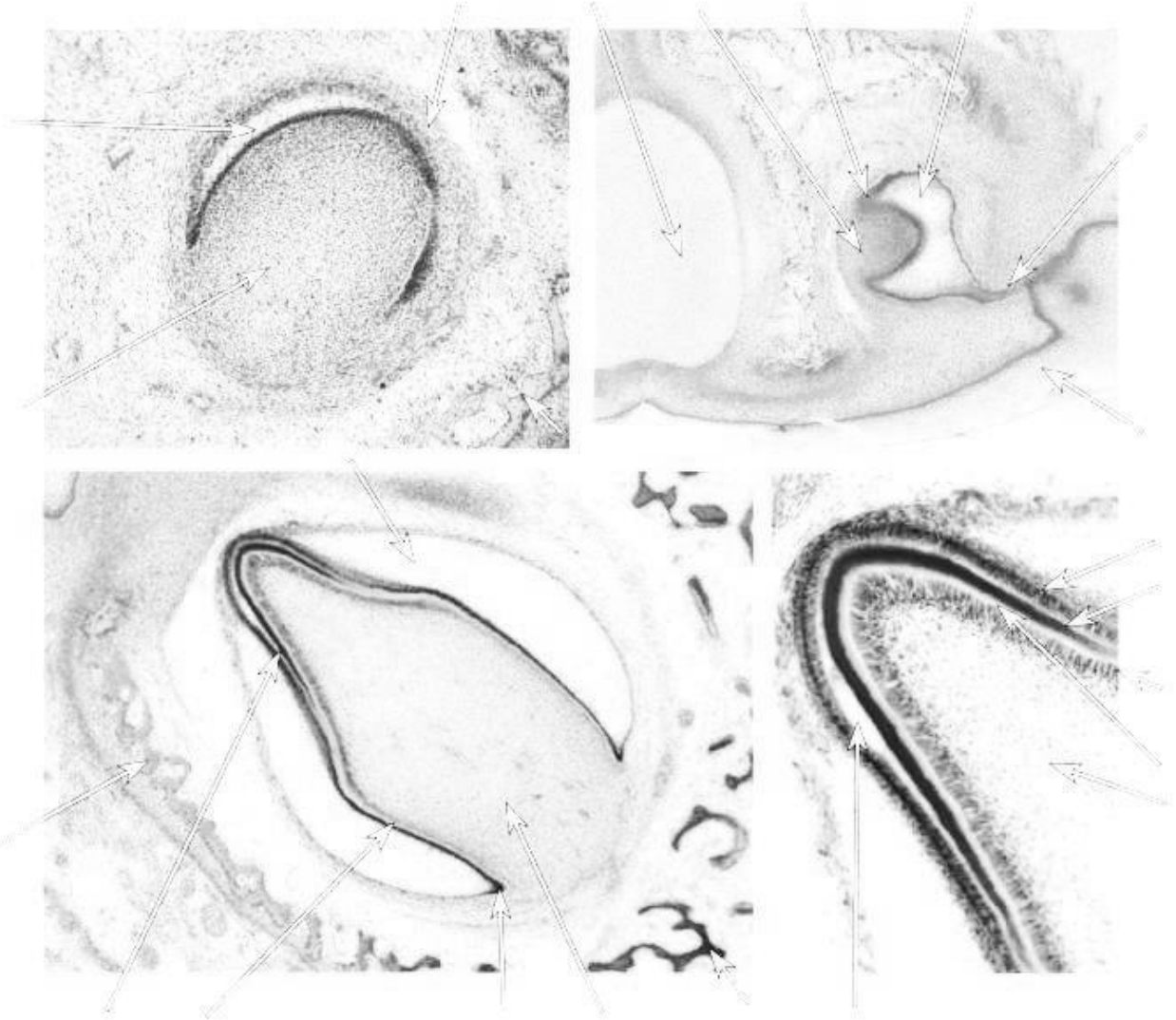
Figure 92. Schematic diagram of tooth development. I - bud stage, II - cap stage, III - early bell stage, IV - late bell stage, Y, VI - maturation; 1 - tooth bud, 2 - dental papilla, 3 - inner enamel epithelium, 4 - outer enamel epithelium, 5 — enamel, 6 - dentin, 7 — dental pulp, 8 - periodontal ligament

Maturation (crown stage) Hard tissues, including enamel and dentin, develop during this stage of tooth development. Dentinogenesis Dentin formation is the first identifiable feature in the crown stage of tooth development. **Odontoblasts,** the dentin-forming cells, differentiate from cells of the dental papilla. They begin secreting an organic matrix, which contains collagen fibers, around the area directly adjacent to the inner enamel epithelium. Further odontoblasts begin to move toward the center of the tooth, forming an extension called the odontoblast processes. Amelogenesis is the formation of enamel on teeth and occurs during the crown stage of tooth development after dentinogenesis. Cementogenesis occurs late in the development of teeth. The cementoblasts differentiate from cells of dental follicle. The cementoblasts secrete matrix of proteins and collagen fibers. Then mineralization takes place.

Practical lessons

1.Development of the tooth. Early stage.
2. Development of the tooth. Later stage.
3. Chronology of tooth development and order of eruption.
4. Tooth enamel: microscopic and chemical compounds.
5. Tooth dentine: microscopic and chemical compounds.
6. Tooth cementum: microscopic and chemical compounds.
7. Structure and functions of tooth pulp and periodontum. Parodontium.

Paint and mark basic histological structure



Signature of teacher_____

Salivary glands

The major salivary glands are paired organs with long ducts that empty into the oral cavity. These are three pairs of major salivary glands, the parotid, submandibular and sublingual, and numerous small glands situated in the mucosa of the lips, cheeks, tongue and palate. **The functions of the salivary glands** :

- digestive (to wet and lubricate the oral cavity and its contents, to initiate the digestion of carbohydrates);
- immunologic (to secrete IgA, lysozyme, lactoferrin);
- excretive (to excrete products of a metabolism, medicine, heavy metals); regulation of a water-salt homeostasis (to excrete of the liquid containing ions Na, K, Ca, Cl);
- endocrine (to secrete of an active substances: parotin, the factor of growth of nerves, the epidermal factor of growth, etc).

General plan of the structure of the large salivary glands The large salivary glands are compound tubulo-alveolar glands. The large salivary gland is covered by connective tissue capsule; septa divide the gland into lobules.

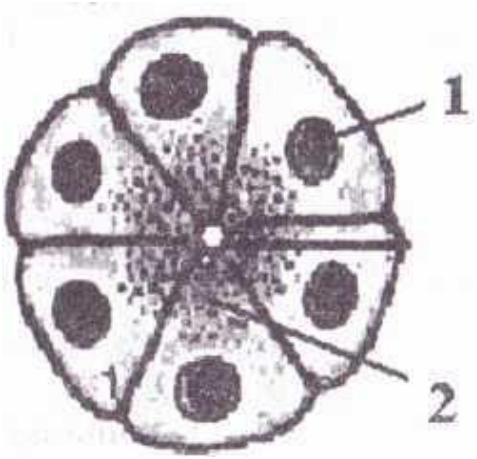
Major salivary gland consists of:

- **secretory portion,**
- **duct system**.

The secretory portion consists of two general types of cells:

1) secretory (serous and mucous) and

2) myoepithelial cells. Serous cells (fig.93) are pyramidal in shape, with a broad base resting on the basal lamina and a narrow apical surface facing the lumen.



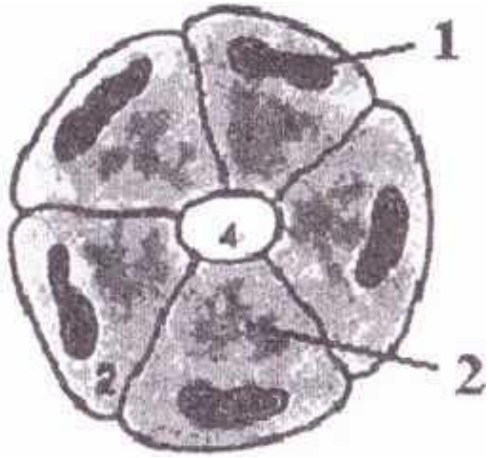


Fig.93. Serous cells of the salivary gland gland. Fig.94 Mucous cells of the salivary 1 -nucleus1 — nucleus, 2 - granules of mucinogen

They have characteristics of polarized protein-secreting cells. Nuclei are spherical and placed near the centre of the cell. The basal part of cytoplasm takes a deep basic stain due to rough endoplasmic reticulum. The supranuclear part contains large serous granules. Mucous cells (fig.94) are cells are large, pale with oval nuclei in the basal parts. The cytoplasm contains large mucinogen granules. Myoepithelial (basket) cells (fig.95) have many long cytoplasmic processes and surround serous acini, mucous tubules, and intercalated ducts. These cells are of

epithelial origin but contain myofibrils in their cytoplasm and help in the expulsion of secretion.

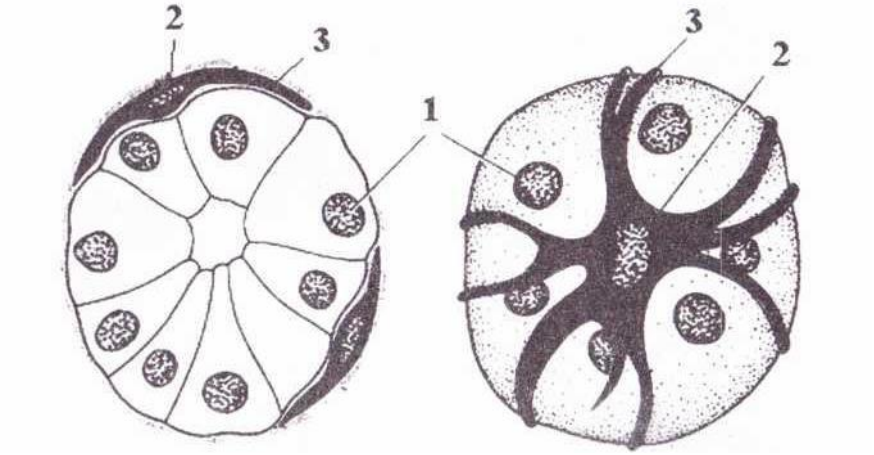


Fig.95. Myoepithelial (basket) cells. 1 — nuclei of the secretory cells, 2 — nuclei of the myoepithelial cells, 3 — processes of the myoepithelial cells (from K). H.Afpanacbee, H.A.IOpwta u dp., 1999)

3 types of the secretory portion are described (fig.96):
1) serous acini (alveoli) which consist of only serous cells;
2) mucous tubules consisting of only of mucous cells and are tubular;
3) mixed acini which consist of both types of secretory cell: serous cells form caps (demilunes of Gianuzzi) surrounding the terminal part of the mucous cells.

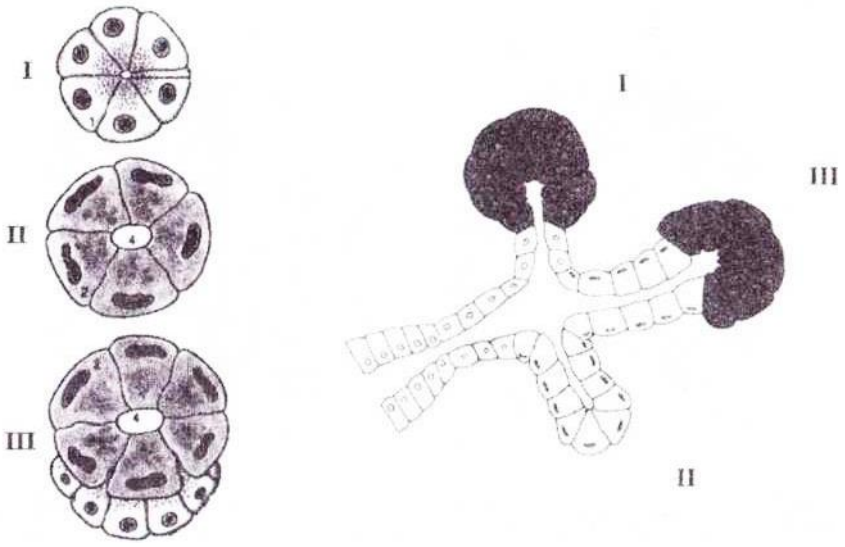


Fig.96. Secretory portions of the large salivary glands. I — serous, IImucous, III - mixed

The duct system consists of:
1) intercalated ducts lead from acini; are lined by simple cuboidal epithelium;
2) intralobular, or striated, ducts are lined by simple columnar epithelium and characterized by radial striations that extend from the bases of the cells to the level of the nuclei; the “striations” consist of infolding of the basal plasma membrane with numerous elongated mitochondria aligned parallel to the infolded membranes;

3) interlobular, or excretory, ducts are lined by stratified cuboidal or columnar epithelium;
4) main duct of each major salivary gland empties into the oral cavity and is lined by stratified squamous nonkeratinized epithelium.

The features of structure of major parotid glands. Parotid gland is a branched acinar gland and contains exclusively serous secretory portions (serous acini). The secretion of this gland is rich in proteins and has a high amylase activity. Submandibular (submaxillary) gland is a branched tubuloacinar gland and contains serous (predominant) and mixed secretory portions. Sublingual gland is a branched tubuloacinar and contains mixed (predominant), mucous, and serous (not numerous) secretory portions. Saliva The saliva is mixed secretion from major and small salivary glands. The salivary glands produce about 1200 mL of saliva a day. Human saliva is composed of 98% water, 2%• electrolytes (Na+ , K+ , CaH , Mg"\ Cl , HC03 ,P043 ,1); • mucus; • antibacterial compounds (lysozyme, salivary lactoperoxidase, lactoferrin, immunoglobulin A); • Epidermal growth factor or EGF; • various enzymes (a-amylase, lingual lipase); • cells (possibly as much as 8 million human and 500 million bacterial cells per mL); • opiorphin, a newly researched pain-killing substance.

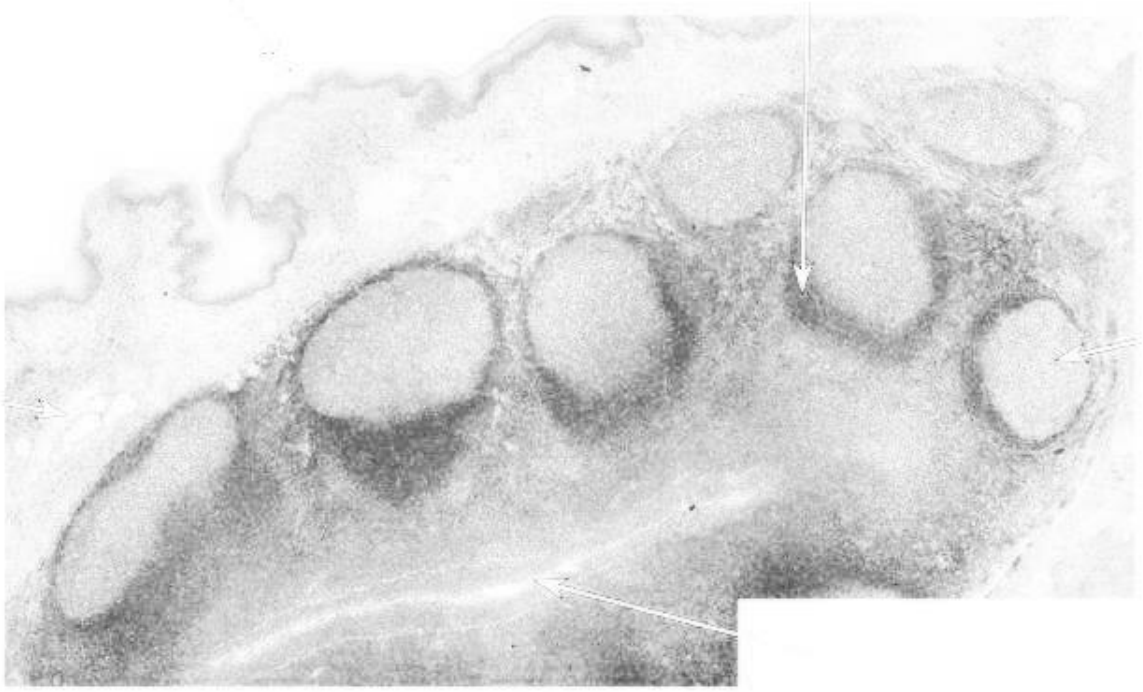
Functions of the saliva

- Moistening dry foods to aid swallowing.
- Providing a medium for dissolved and suspended food materials that chemically stimulate taste buds.
- Buffering of the contents of the oral cavity through its high concentration of bicarbonate ion.
- Digestion of carbohydrates by the digestive enzyme a-amylase.
- Controlling the bacterial flora because of the presence of the antibacterial enzyme lysozyme.
- Source of calcium and phosphate ions essential for normal tooth maintenance

Practical lessons

1.Large salivary glands. Classification, structure, histophysiology, exo- and endocrine functions. Parotid glands.
2. Large salivary glands. Classification, structure, histophysiology, exo- and endocrine functions. Submandibular and sublingual glands.
3. Pirogov’s lymphoepithelial ring. Tonsilles: structure and functions.

Paint and mark basic histological structure

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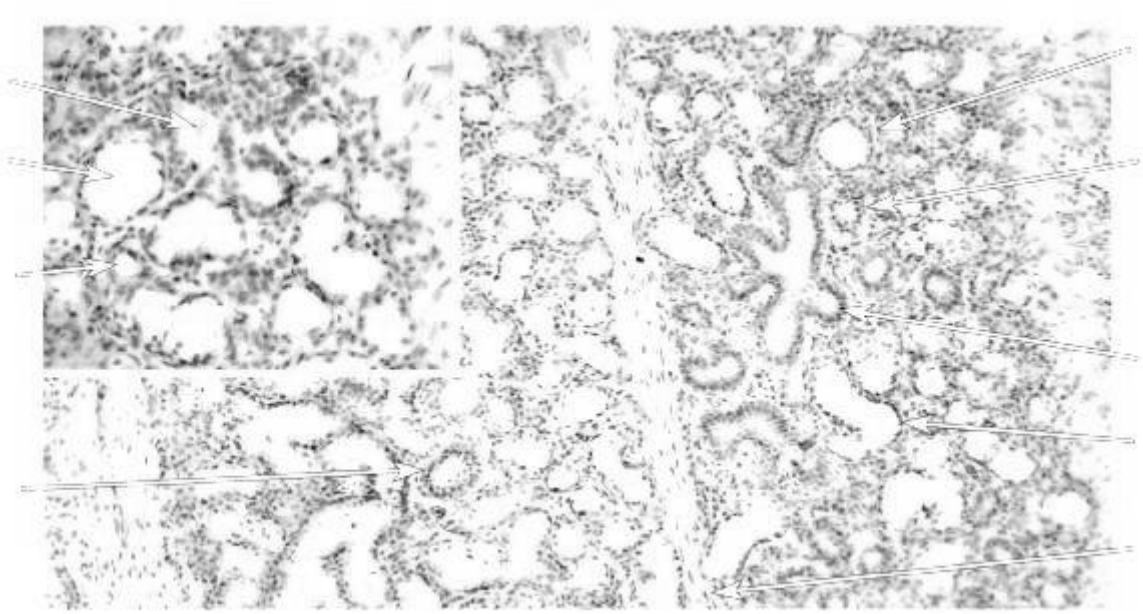

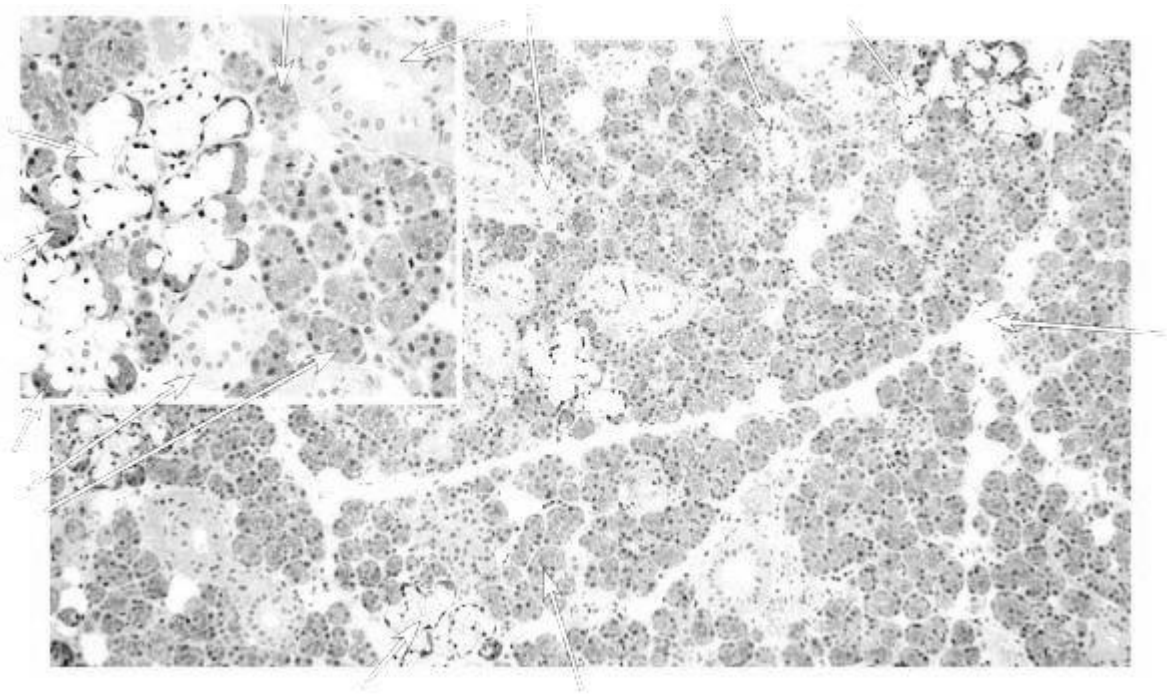

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DIGESTIVE SYSTEM II. PHARYNX. ESOPHAGUS. GASTROINTESTINAL TRACT

Pharynx The pharynx is a common passage for food and air.

Pharynx is divided into 3 parts: nasopharynx, oropharynx and laryngopharynx. **The wall of the pharynx has 4 layers**:

I. **Mucosa consists** of:

1) epithelium is pseudostratified columnar ciliated in nasopharynx and stratified squamous nonkeratinised in oropharynx and laryngopharynx;

2) lamina propria consists of loose connective tissue, contains serous and mucous glands and aggregations of lymphoid tissue.

II. Submucosa consists of loose connective tissue, contains the lymphoid tissue of pharyngeal tonsil in the posterior wall and tubal tonsils in the lateral wall of nasopharynx, and palatine tonsil in the lateral wall of oropharynx.

III. Muscularis consists of two layers of skeletal muscle tissue.

V. Adventitia consists of a loose connective tissue.

Esophagus. The esophagus is muscular tube 25cm long that carries food from phamx to stomach. **The wall of the esophagus has 4 layers** (fig.97):

I. **Mucosae** consists of

1) epithelium is stratified squamous nonkeratinized;

2) lamina propria consists of loose connective tissue, contains the branched tubular esophageal cardiac glands in the region near the stomach;

3) muscularis mucosae contains longitudinal layer of smooth muscle tissue;

II. Submucosae consists of loose connective tissue, contains the secretory parts of the mucous esophageal glands proper;

II. Muscularis has an outer longitudinal and an inner circular layers; in the upper 1/3 of the esophagus the muscular layer consists of only striated muscle fibers; in the middle 1/3 - a mixture of striated and smooth muscle tissue; and in the lower 1/3 - only smooth muscle tissue.

III. IV. External tunic'. in the peritoneal cavity esophagus is covered by serosa which consists of loose connective tissue and a simple squamous epithelium (mesothelium); in the thoracic cavity esophagus is covered by adventitia which consist of loose connective tissue.

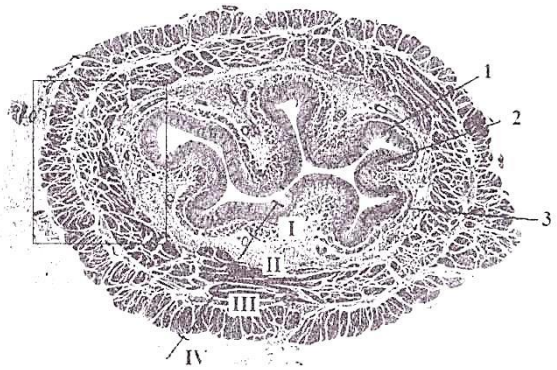


Fig.97. Photomicrograph of the esophagus (cross section). I - mucosa: 1 - epithelium, 2 — lamina propria, 3 - muscularis mucosa; II — submucosa, III — muscularis, IV - adventitia

Stomach. The stomach is the dilated segment of the digestive tract which receives food from the esophagus, undergoes mechanical and chemical breakdown to form chyme. **The functions of the stomach**

- to transform the ingested food by muscular activity into a viscous mass (chyme) and progress it to the distal part of gastro-intestinal tract;
- to continue the digestion of carbohydrates initiated in the mouth, promote the initial digestion of protein and lipids with the enzymes pepsin and gastric lipase;
- to product of intrinsic factor, which is essential for vitamin B_{12} absorption;
- absorption of some substances such as water, salt sugar and other;
- endocrine secretion.
- **Stomach has 4 regions**:
- cardia,
- fundus,
- body and pylorus (fig-98). Because the fundus and body are identical in microscopic structure the stomach has such **histological parts:**
- cardiac;
- fundic;
- pyloric.

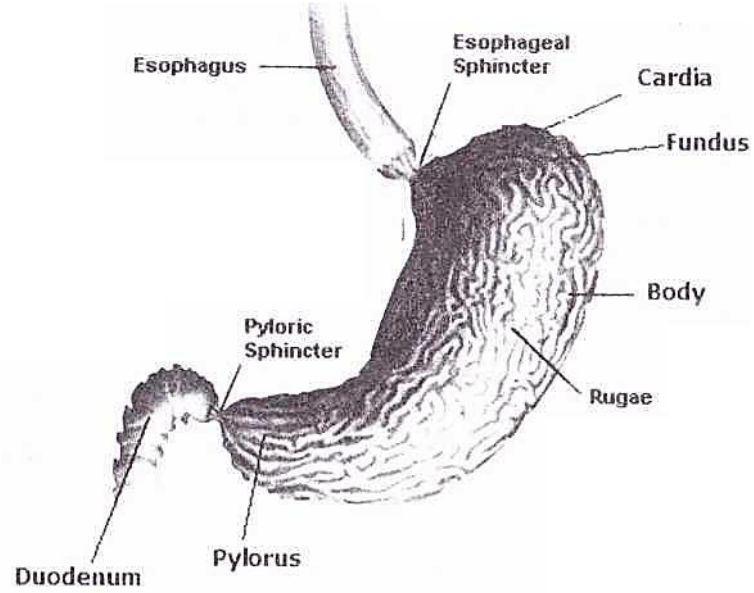


Figure 98.Regions of the stomach.

The wall of the stomach consists of the 4 layers (fig.99):

I. Mucosa;
II. II. Submucosa;
III. III.Muscularis
IV. IV.Serosa.

Gastric mucosa has a complex relief:

- longitudinal folds or ridges termed rugae composed of the mucosa and submucosa;
- gastric pits (foveolae) are the invaginations of the epithelium into the lamina propria which serve as the ducts of gastric glands;

- mamillated areas - bulging irregular areas formed by grooves or shallow trenches.

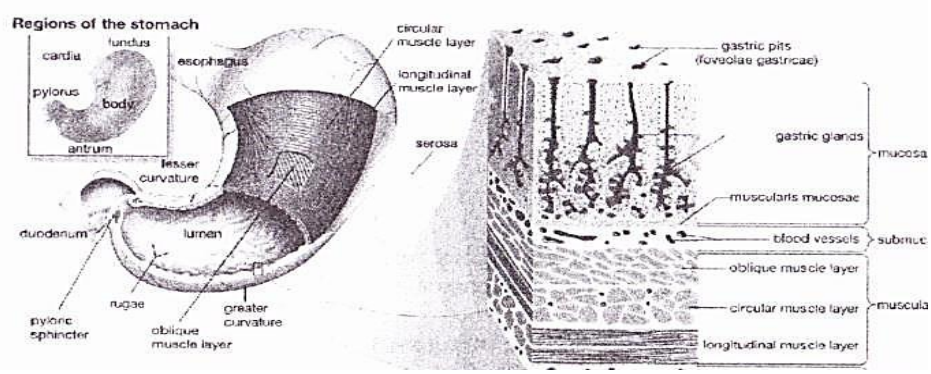


Figure 99. Structure of stomach wall.

I.Gastric mucosa consists of:

1) surface epithelium is simple columnar and mucous secreting;

2) lamina propria is composed of loose connective tissue; it is packed gastric glands;

3) muscularis mucosae is well developed, consists of three layers of smooth muscle cells.

II. Submucosa consists of loose connective tissue, blood vessels and submuscular nerve plexus.

III.Muscularis is composed of smooth muscle cells oriented in three layers, an middle layer is greatly thickened to form the pyloric sphincter.

IV. Serosa consists of a layer of squamous cells (mesothelium) with a small amount of underlying connective tissue.

Glands in the lamina propria empty into the bases of the gastric pits. The stomach is divided into three histological regions based on the nature of the glands.

1) . The cardiac region is a narrow band near the opening of the esophagus, which contains cardiac glands. Cardiac glands are composed almost entirely of mucus-secreting cells, with the odd enteroendocrine cell present. These glands may branch and frequently coil at their terminal part. Their secretion protects the esophagus against gastric reflux. Gastric pits in the cardiac region are fairly shallow.

2) . The fundic region constitutes the majority of the stomach. The glands in this region are known as gastric or fundic glands and extend all the way to the muscularis mucosae. 3-7 glands open into the base of each gastric pit. Each gland has long, narrow neck and a short, wider base (fig.100). At their base, the glands may divide into two or three branches which become slightly coiled.

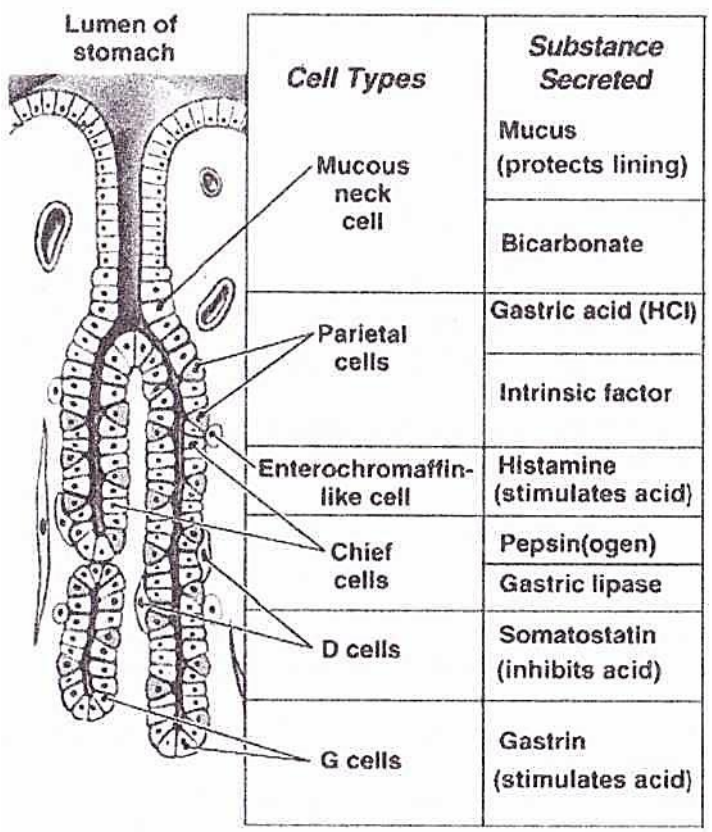


Figure 100. Schematic diagram of the gastric gland. 1 - gastric pit, 2 - mucus cells, 3 - parietal cells, 4 - chief cells, 5 - enteroendocrine cells.

The following cells types can be seen in the glands of the fundic region:

- **Mucous neck cells** are located in the neck region and secrete a mucous.
- **Parietal (or oxyntic)** cells (fig.101) are found predominantly in the upper part of the gland. They secrete HCl and intrinsic factor. They are intensely eosinophilic due to the amount of membrane comprising an extensive intracellular canalicular system and numerous mitochondria. HCl secretion is stimulated mainly by gastrin. Intrinsic factor is a glycoprotein that binds vitamin $B|_{12}$, essential for maturation of red blood cells.
- **Chief cells** are located mainly near the base of the glands and are typical protein-secreting cells. Their basophilia stems from their abundant rER. They secrete pepsinogen and lipase. Pepsinogen is converted to the proteolytic enzyme pepsin upon contact with the acidic gastric juice.
- **Enteroendocrine cells** are more prevalent near the base of gland. Enteroendocrine cells secrete their product into the lamina propria whence it is taken up by blood vessels. The major secretory product of the enteroendocrine cells of the stomach is gastrin, which stimulates the production of HC1. Other products are glucagon, serotonin, substance P and VIP.

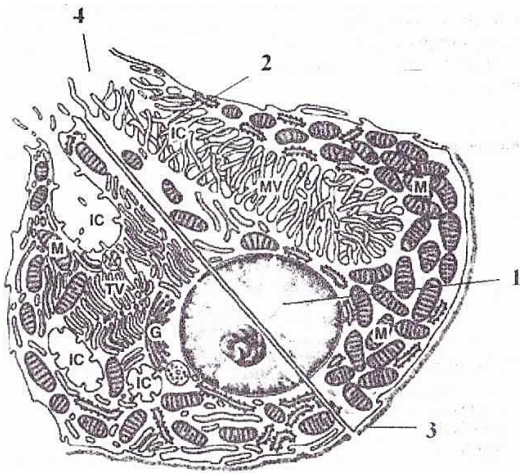


Figure 101. Schematic diagram of the parietal (oxyntic) cell. 1 - nucleus, 2 intracellular canaliculus, 3 - basal lamina, 4 – lumen.

other cell types. They are low columnar cells. They travel upwards to replace surface mucous cells whose lifespan is 3-5 days, and downward to replace parietal, chief and enteroendocrine cells, whose lifespan is about a year.

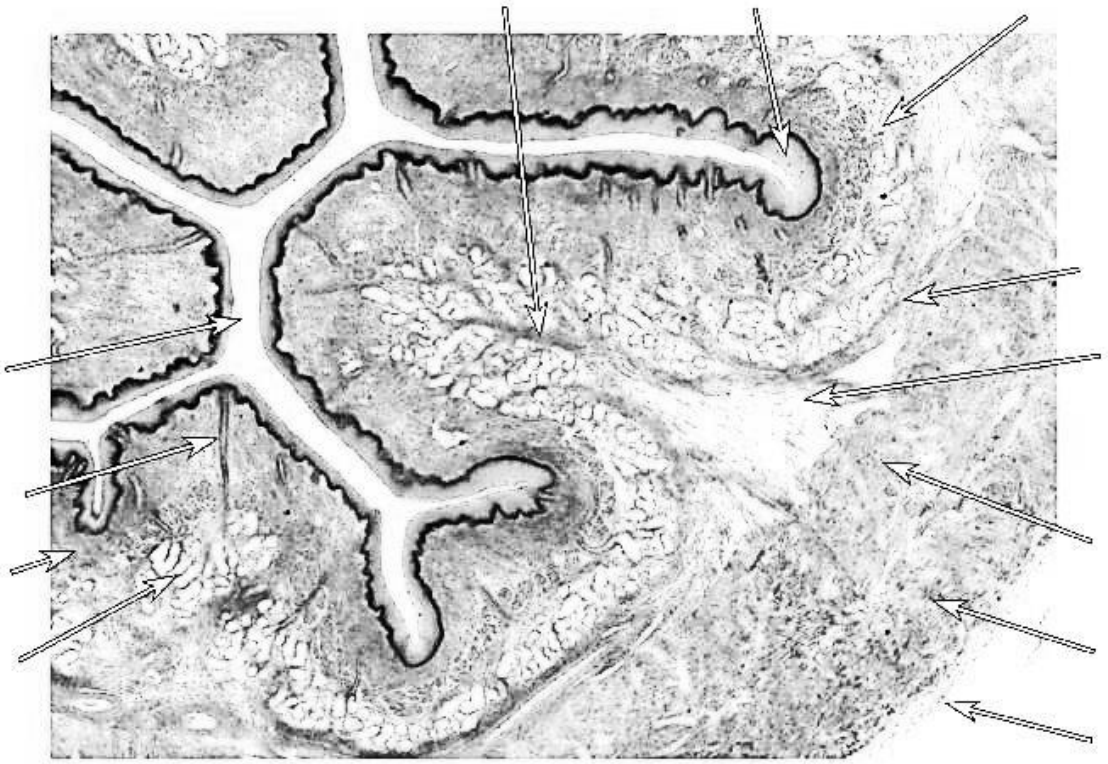
3) . **The pyloric region is the part of the stomach proximal** to the pyloric sphincter, and contains pyloric glands. These are short, coiled, branched tubular glands with a wide lumen. Their cells secrete mucous and are similar in appearance to the surface mucous cells. The gastric pits in this region are very deep, going about halfway down to the muscularis mucosae. Gastric glands secrete gastric juice. Gastric juice is a watery secretion w'ith Ph 0,9-1,5. The components of gastric juice are:

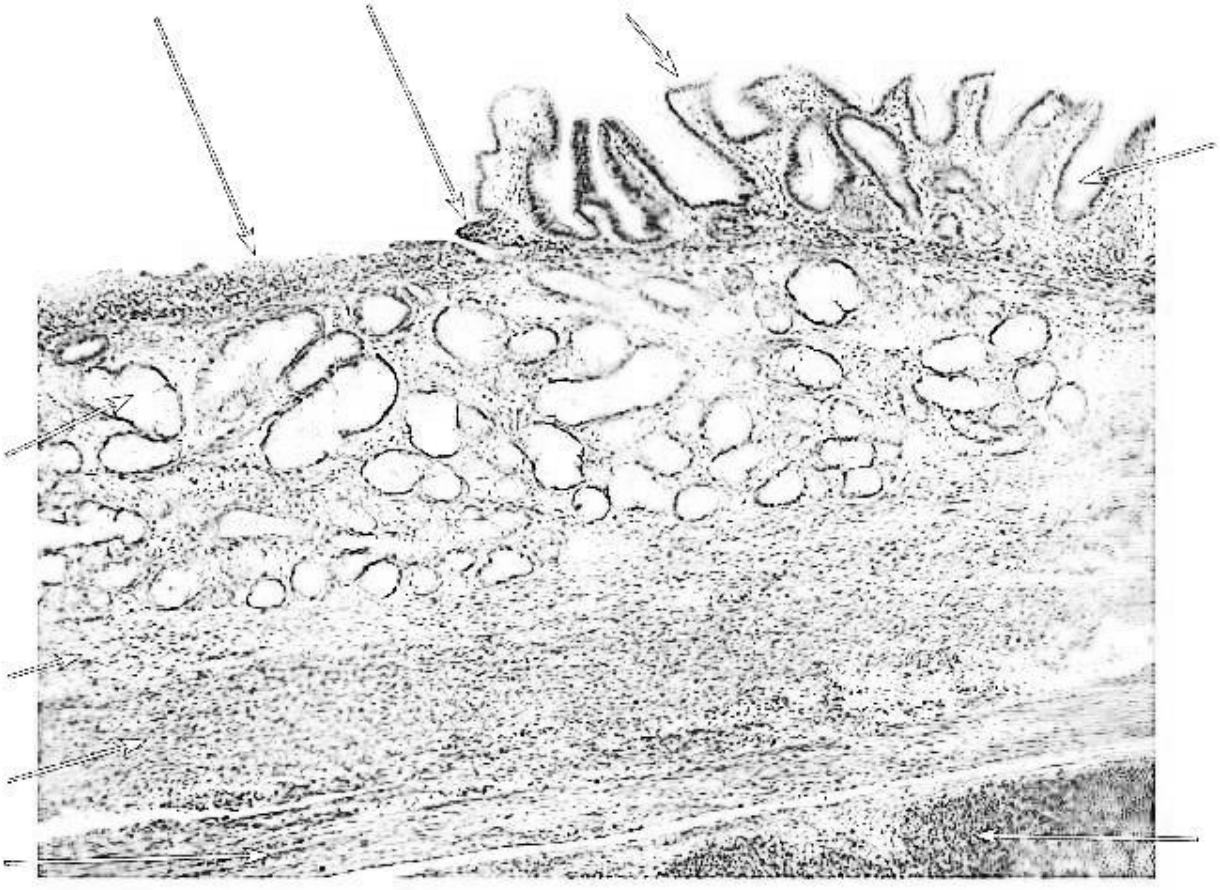
- hydrochloric acid (HC1) is produced by parietal cells; it converts inactive pepsinogen into the active enzyme pepsin;
- pepsin is proteolytic enzyme;
- mucus is acid-protective coating for the gastric mucosa; > intrinsic factor binds to vitamin B_{12}; it is essential for absorption of vitamin B_{12} which occurs in the distal part of the ileum.

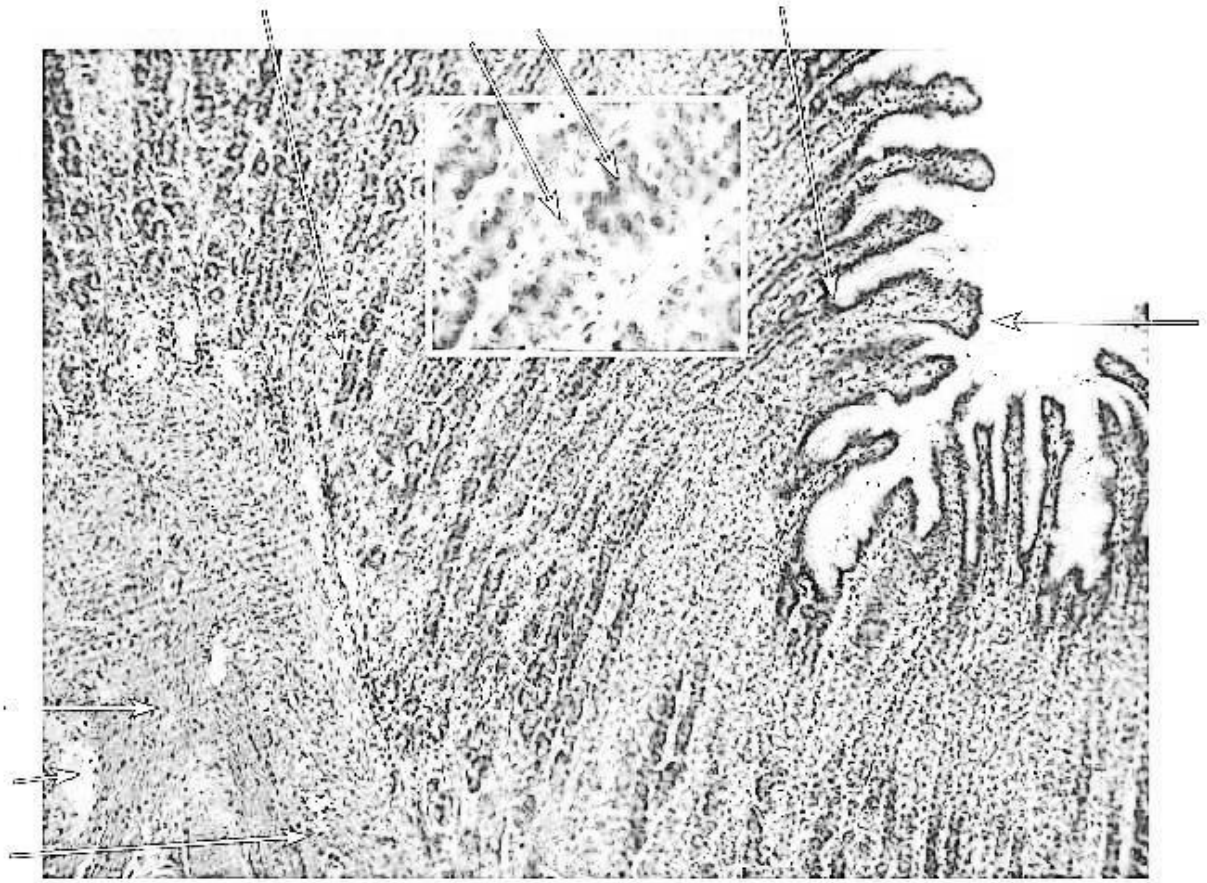
Practical lessons

1. Pharynx and esophagus. General structure and microscopic peculiarities of the different portions of esophageal wall.
2. Stomach: walls, structure and tissues compounds. Stomach glands: disposition, structure and cell compounds (exo- and endocrine cells types). Secretory cells (histophysiology).

Paint and mark basic histological structure







Signature of teacher_____

Small intestine The small intestine is the longest component of the digestive tract (over 6 m), is divided into three portions: duodenum, jejunum, ileum. The functions of the small intestine:

- terminal food digestion;
- nutrient absorption;
- mechanical (to progress of the contents to the distal part of the large intestine);
- endocrine secretion;
- immune defence.

The wall of the small intestine consists of 4 layers:

I. mucosa;
II. submucosa;
III. muscularis;
IV. serosa or adventitia.

The relief of mucosa of the small intestine:

- folds (plicae circularis), consisting of mucosa and submucosa;
- intestinal villi are fingerlike surface projections of the mucosa into the lumen of the small intestine;
- intestinal glands (crypts of Lieberkuhn) are invaginations of the epithelium into lamina propria (the simple tubular glands).

I. Mucosa consists of:

1) simple columnar epithelium;
2) lamina propria is composed of loose connective containing tissue with blood vessels, nerves and smooth muscle cells; these cells are responsible for the rhythmic movements of the villi, which are important for absorption; lamina propria contains aggregates of lymphoid tissue which is termed as gutassociated lymphoid tissue (GALT);
3) muscularis mucosae consists of smooth muscle cells. **The intestinal epithelium consists of some types of cells:**
enterocytes (absorptive cells),
goblet cells,
Paneth's cells,
enteroendocrine cells,
M (microfold) cells,
stem (undifferentiated) cells.
Enterocytes (fig.102) are tall columnar cells, with oval nuclei in the basal half of the cell, specialized for the transport of substances. In the apex of each cell there is the striated (brush) border of closely packed microvilli, which greatly increase the surface area for absorption. Amino acids and monosaccharides are absorbed by active transport, monoglycerides and fatty acids cross the microvilli membranes passively. Absorbed substances enter either the fenestrated capillaries in the lamina propria just below the epithelium, or the lymphatic lacteal (most lipids and lipoprotein particles).

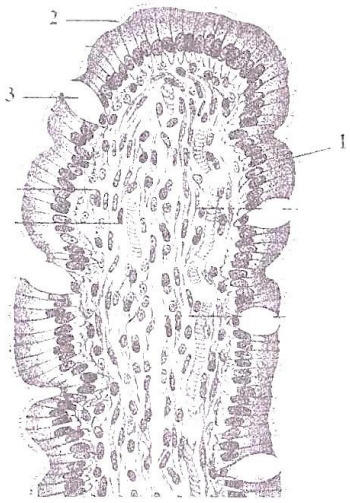


Figure 102. Schematic diagram of the villus. ' 1 — enterocytes, 2 - striated border, 3 - goblet cells

Goblet cells are found interspersed among the absorptive cells. They are unicellular mucus secreting glands. The slender base of the cell contains the nucleus and organelles. Goblet cells usually appear pale or empty due to the loss of their contents upon preparation. They progressively increase in number from the proximal to distal part of intestine. The main function of the gobiet mucus is to protect and lubricate the lining of the intestine.

Paneth's celts are pyramidal cells that present only at the bases of intestinal glands. These exocrine cells contain large acidophilic granules in the apical cytoplasm; the basal cytoplasm is basophilic. The granules contain the antibacterial enzyme lysozyme. Lysozyme is the enzyme that digests the cell wall of some bacteria. Paneth's cells also phagocytise some bacteria and protozoa.

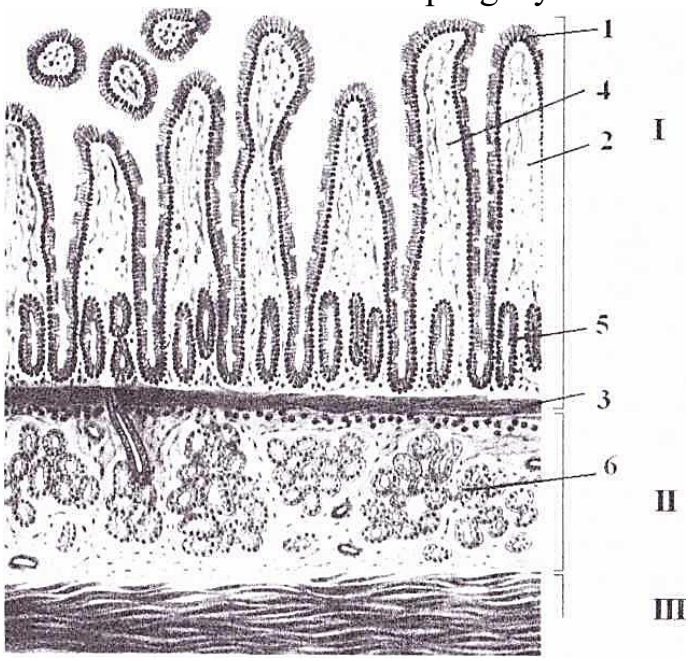


Figure 103. Diagram of structure of duodenum. I - mucosa: 1 - epithelium, 2 - lamina propria, 3 - muscularis mucosae, 4 - villus, 5 - crypt, II - submucosa: 6 - duodenal glands of Brunner, III - muscularis

They may have a role in regulating intestinal flora**.**

Enteroendocrine cells are most often found in the lower part of the crypts but can occur at all levels of the epithelium. Their most abundant products are cholecystokinin (CCK), which stimulates pancreatic enzyme secretion and gall bladder contraction, secretin, which stimulates pancreatic and biliary bicarbonate secretion, and gastric inhibitory peptide (GfP), which inhibits gastric acid secretion. Mor microfold cells overlie Peyer's patches and other large lymphatic aggregations. They endocytize antigens and transport them to the underlying lymphoid cells where immune responses to foreign antigens can be initiated. M - cells represent an important link in the intestinal immune system. Stem (undifferentiated) cells are situated in depth of the intestinal crypts, they are similar to absorptive cells, but their microvilli are not so well developed. Stem cells proliferate actively by mitosis. The new-formed cells migrate upwards from the crypt to reach the walls of villi and differentiate into absorptive or goblet cells. II. Submucosa consists of a loose connective tissue, contains aggregates of lymphoid tissue known as Peyer's patches. In the submucosa of the duodenum there are duodenal glands of Brunner; these are compound tubular mucous glands. III. Muscularis is composed of 2 layers of smooth muscle tissue. IV. Either a serosa or an adventitia may be present.

Large intestine. The large intestine consists of the colon, cecum, appendix, rectum and anal canal. **The functions of the large intestine:**

- Absorption of water and electrolytes.
- Elimination of undigested food and waste.
- Mechanical (to progress of the contents to the distal part of the large intestine).
- Absorption of vitamins K and B.
- Endocrine secretion.
- Immune defence.

The wall of the large intestine consists of 4 layers (fig.104):

I. mucosa;
II. submucosa;
III. muscularis;
IV. serosa or adventitia. The relief of mucosa of the large intestine: > semilunaris folds consisting of mucosa and submucosa; > intestinal glands (crypts) are straight, tubular, contain a great abundance of goblet and absorptive cells and small number of cnteroendocrine cells.

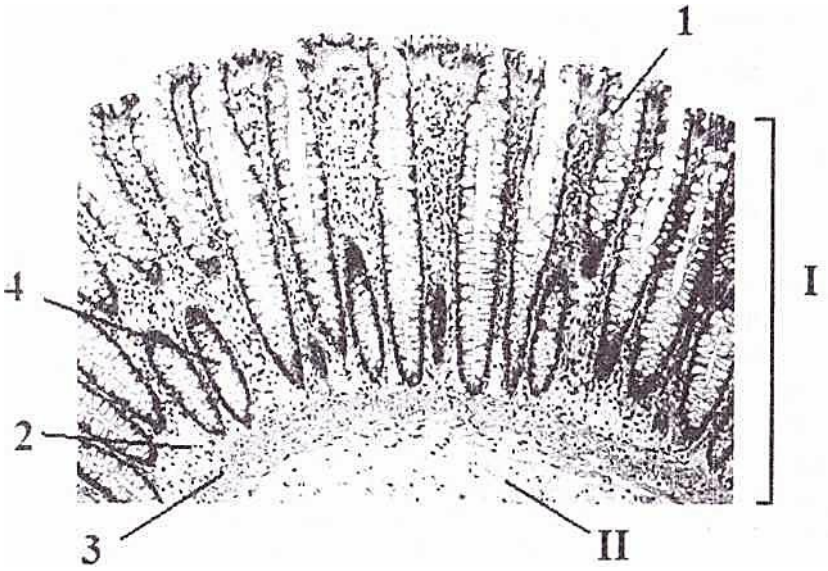


Figure 104. Photomicrograph of the large intestine. I - mucosa: 1 — epithelium, 2 - lamina propria, 3 - lamina muscularis, 4 - crypts; II – submucosa.

The relief of mucosa of the large intestine:
-semilunaris folds consisting of mucosa and submucosa;
-intestinal glands (crypts) are straight, tubular, contain a great abundance of goblet and absorptive cells and small number of cnteroendocrine cells.

Mucosa consists of:

1) simple columnar epithelium;
2) lamina propria is composed of loose connective tissue, it is rich in lymphoid cells and lymph nodules; extensive development of GALT reflects the abundance and variety of microorganisms and noxious end products of metabolism;
3) muscularis mucosae consists of smooth muscle tissue, has a circular and longitudinal layer. Epithelium consists of some types of cells:
- absorptive cells,

- goblet cells,
- stem (undifferentiated) cells,
- enteroendocrine cells.

Absorptive cells are tall columnar and have short, irregular microvilli. The absorptive cells actively transport electrolytes. Water is also absorbed as it passively follows the electrolytes. Goblet cells are more prevalent in the crypts than along the surface, and their number increases distally toward the rectum. The mucus facilitates the passage of the colonic contents, and covers bacteria and particulate matter. **Stem** (undifferentiated) cells are located at the bases of the crypts. Epithelium of the large intestine is replaced about every 6 days by the proliferation and differentiation of these cells. Enteroendocrine cells are rare.

Submucosa consists of a loose connective tissue. It is rich in lymphoid follicles (nodules).

Muscularis consists of an inner circular and outer longitudinal layer of smooth muscle tissue. The inner circular layer is typical, but the outer longitudinal layer of the colon is very thin, except for three extremely thick longitudinal bands, called teniae coli.

Serosa consists of mesothelium with and thin layer of underlying connective tissue, is characterized by small protuberances composed of adipose tissue - the appendices epiploicae.

Appendix The appendix is an evagination of the cecum; it is characterized by small, narrow lumen that is caused by the presence of abundant lymphoid follicles in its wr all. The general structure of the appendix is similar to that of the large intestine.**mucosa;**

1) simple columnar epithelium;
2) lamina propria is composed of loose connective tissue containing with blood vessels, nerves and smooth muscle cells; these cells are responsible for the rhythmic movements of the villi, which are important for absorption; lamina propria contains aggregates of lymphoid tissue which is termed as gutassociated lymphoid tissue (GALT);
3) muscularis mucosae absent (non-available)

- **submucosa;**
- **muscularis;**
- **serosa** has its own ripples.

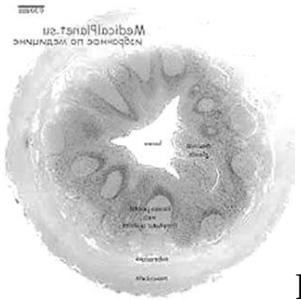
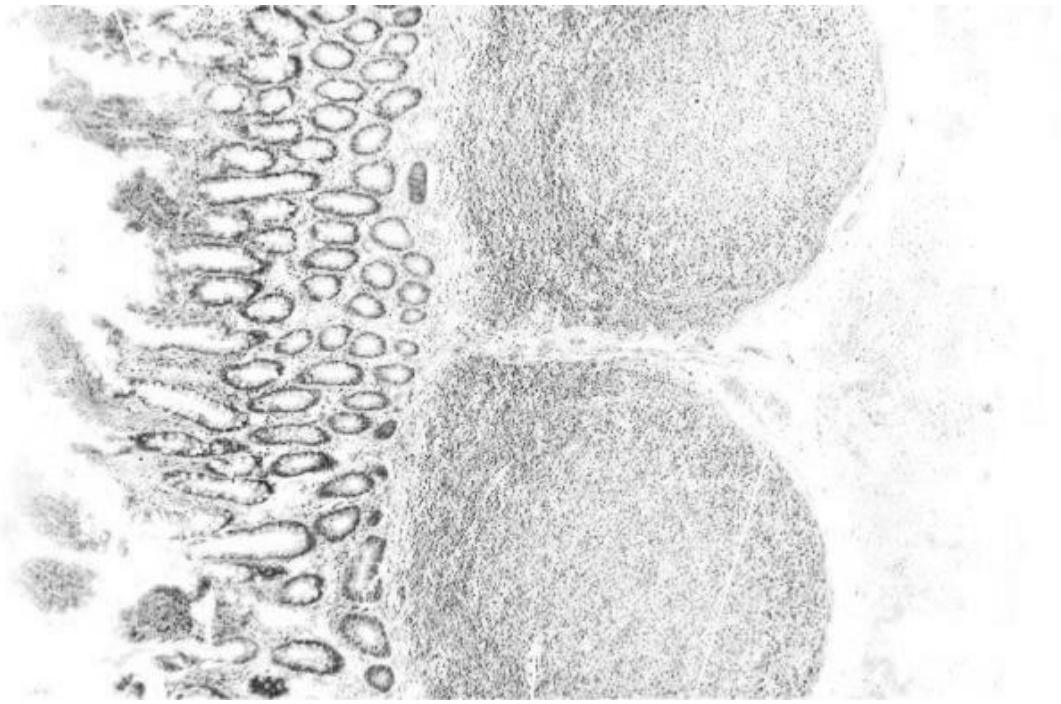


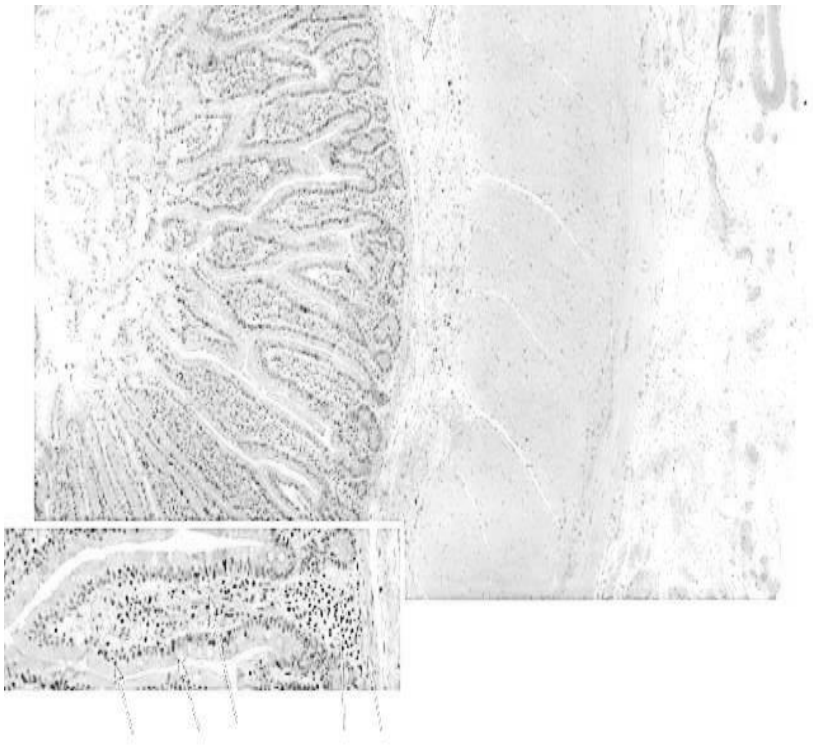
Figure 105. **Appendix**

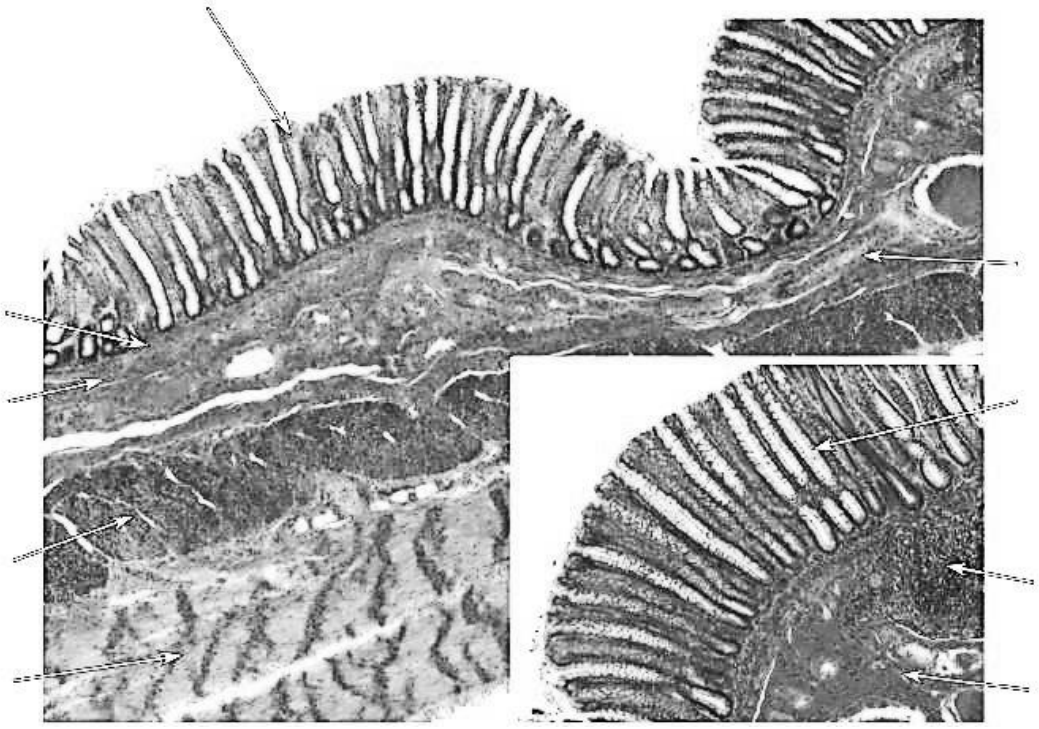
Practical lessons

1. Small intestine. Structure and functions. “Cript-villus” sytem: histophysiology and their participation in the parietal and intracavitary digestion.
2. Large intestine. Structure and functions. Appendage: structure and function.
3. Rectum. Portions and their peculiarities.

Paint and mark basic histological structure







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DIGESTIVE SYSTEM III. PANCREAS. LIVER. GALLBLADDER

Pancreas The pancreas is both an exocrine and endocrine gland. The exocrine part produces about 1.5 L of pancreatic juice every day. **The endocrine part**, which accounts for -1-2% of the pancreas, consists of the clusters of cells of the endocrine tissue known as islets of Langerhuns. These cells produce insulin, glucagon and a number of other hormones. The pancreas is covered by a **thin capsule** of connective tissue that sends septa into it, dividing the pancreatic lobules.

Exocrine pancreas. The exocrine pancreas secretes digestive enzymes that can digest most food substances:

- proteolytic endopeptidases (trypsinogen, chymotrypsinogen) and
- proteolytic exopeptidases (procarboxypeptidase, proaminopeptidase) digest proteins into smaller peptides or amino acids;
- amylolytic enzymes (a-amylase) digest carbohydrates into to glucose and small saccharides;
- lipases (triacylglycerol lipase, phospholipase) hydrolyses triglycerides into fatty acids and monoglycerides;

- nucleolytic enzymes (deoxyribonuclease, ribonuclease) digest nucleic acids producing mononucleotids. The exocrine pancreas constitutes main part of gland (97%). It is compound serous tubuloacinar gland, which consists of:
- secretory portion (acini),
- duct system.

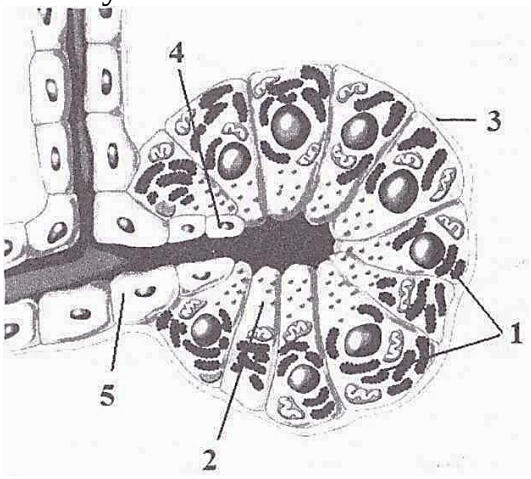


Figure 106. Schematic diagram of the structure of pancreatic acinus. 1 - acinar cells, 2 - zymogen granules, 3 - basal lamina, 4 - centroacinar cells, 5 - intercalated duct

Acini have elongated shape (fig.106), narrow lumen, are composed of **2 types of cells:**
- acinar and
- centroacinar cells.

Acinar cells are highly polarized, with spherical basally located nuclei, the basal cytoplasm is basophilic, consists of rough endoplasmic reticulum, the apical part contains acidophilic zymogen granules. Zymogen granules are secretory vesicles containing the inactive precursors of digestive enzymes. They are activated in the lumen of the digestive canal.

Centroacinar cells are small, flattened with pale cytoplasm, are situated in the centre of acinus. They represent the terminal lining cells of intercalated ducts.

Duct system consists of:
- intercalated duct begins within the acinus, is lined by simple squamous epithelium; these cells secrete fluid and bicarbonate ions of the pancreatic juice; intercalated ducts are short and drain into intralobular ducts;
- intralobular duct is lined by simple cuboidal epithelium; intralobular ducts drain into larger intralobular ducts;
- interlobular ducts are in the septa of the gland; are lined by simple columnar epithelium; intralobular ducts drain directly into main pancreatic duct;
- main pancreatic duct of the gland is lined by tall columnar epithelium.

The main pancreatic duct opens into the summit of the major duodenal papilla, usually in common with the bile duct. A duct draining the lower parts of the head of the pancreas, the accessory pancreatic duct (of Santorini), is very variable. If present, it may open into the minor duodenal papilla ~2 cm above the major papilla in the duodenum.

Endocrine pancreas. The endocrine pancreas is the islets of Langerhans are distributed throughout the organ in cell groupings of varying size. The islets constitute about 1 to 2% of the volume of the pancreas. Polygonal cells of the islets are arranged in short, irregular cords that are profusely invested with a network of fenestrated capillaries. Each cell type of the islet can be correlated with a specific hormone, and each has specific location in the islet (fig.107).

- 75% B (beta)-cells are most numerous, blue-stained, form the central part of the islets, secrete hormone insulin. Insulin decreases blood glucose levels. Its principal effects are on the liver, skeletal muscles, and adipose tissue. Insulin stimulates: • uptake of glucose from the circulation into cells and activates glucokinase in liver cells; • storage of glucose by activation of glycogen syntheses; • phosphorylation and use of glucose by promoting its glycolysis within cells.

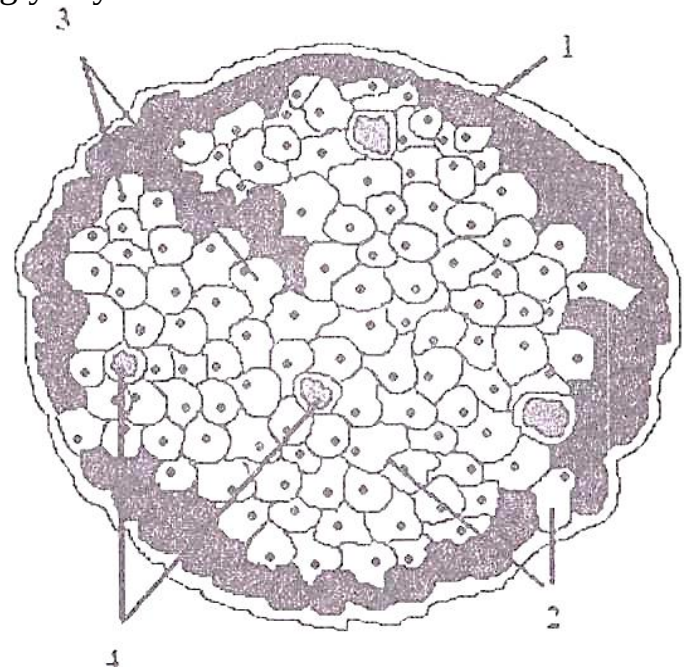


Figure 107. Schematic diagram of the islet of Langerhans. 1 - A (alpha)- cells, 2 - B (beta)-cells, 3-D (delta)-cells, 4 - blood capillaries

- 20% A (alpha)-cells constitute of the islet, are stained pink, are distributed on the periphery of the islets, secrete hormone glucagon. The effects of glucagon are generally opposite to those of insulin. It stimulates release of glucose into the bloodstream, and stimulates gluconeogenesis (synthesis of glucose from metabolites of amino acids) and glycogenolysis (breakdown of glycogen) in the liver.
- 5-10% D (delta)-cells secrete somatostatin, a locally acting hormone which inhibits insulin and glucagon secretion.
- Dl-cells secrete hormone vasoactive intestinal peptide (VIP), which has effects similar to glucagon, but also stimulates the exocrine function of the pancreas.

- PP-cells secrete hormone pancreatic polypeptide (PP), which stimulates chief cell in gastric glands and inhibits bile and bicarbonate secretion. y EC-(enterochromaffin) cells secrete several peptides including: O motilin, which increases gastric and intestinal motility, O secretin, which stimulates I ICO ;' secretion in pancreatic juice and pancreatic enzyme secretion; O substance P. which has neurotransmitter properties. D-, D1-, PP- and EC-celis are present in the islets or else distributed singly or in small groups between the exocrine acini and along the ducts.

Liver. The liver is the largest gland in the body.

The functions of the liver:

- synthesis and endocrine secretion of many plasma proteins (albumins, lipoproteins, glycoproteins, prothrombin and fibrinogen);
- storage of vitamins (A, D, K) and iron;
- detoxification of many drugs and toxins; y metabolic functions (synthesis of urea, metabolism of cholesterol and fat, glycogen synthesis, storage of glycogen, glucogenolysis, gluconeogenesis);
- protective (destruction of microorganisms, toxins brought by the blood);
- production of bile required for emulsifying fats;
- catabolism of hemoglobin from worn-out red blood cells;
- volume reservoir for blood;
- embryonic hematopoiesis (in the first trimester fetus, the liver is the main site of red blood cell production);

The liver is enclosed in a thin connective tissue capsule (Glisson's capsule). The liver receives a dual vascular supply.

All of the blood which passes through the intestine and spleen is delivered to the liver by the hepatic portal vein. This portal blood carries not only nutrients but also various contaminants (drugs, toxins from food, bacteria, by products of blood-cell recycling) which have been absorbed through the intestinal mucosa or produced in the spleen.

The hepatic artery brings fresh, oxygenated blood from the aorta. Portal venous blood from the intestine and spleen and arterial blood from the aorta mix together in hepatic sinusoids before leaving the liver in the hepatic vein. The basic structural component of the liver is the liver cells, or hepatocytes. Structural units of the liver are the liver lobules. Liver lobule is hexagonal prisms in a cross section about 1mm x 2mm (fig.108). Within each lobule, hepatocytes are arranged into hepatic cords one or two cells thick. Hepatic cords are radially disposed in the liver lobule. The cords of hepatocytes represent the parenchyma of the liver. The spaces between the cords contain sinusoidal capillaries (liver sinusoids) lined by a fenestrated endothelium. At the corners of the lobules there are the portal spaces, which are occupied by the portal triads.

The portal triad contains:

1) interlobular vein (a branch of the portal vein):
2) interlobular artery (a branch of the hepatic artery);
3) interlobular bile duct (part of the bile duct system).

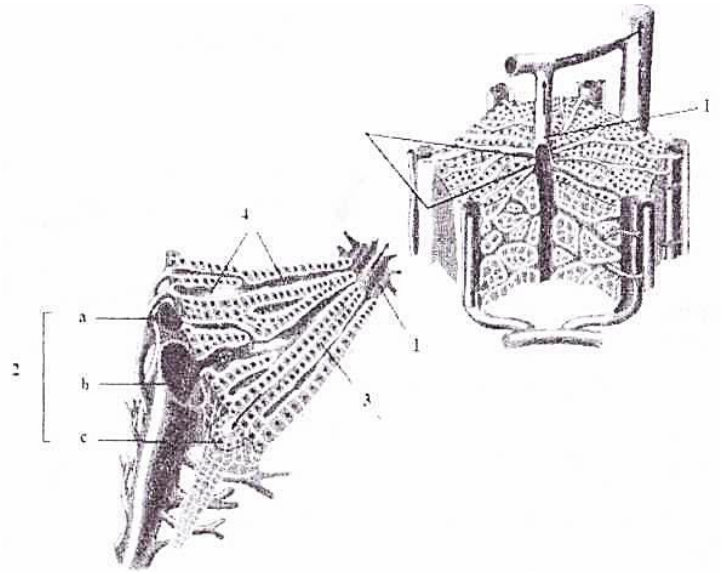
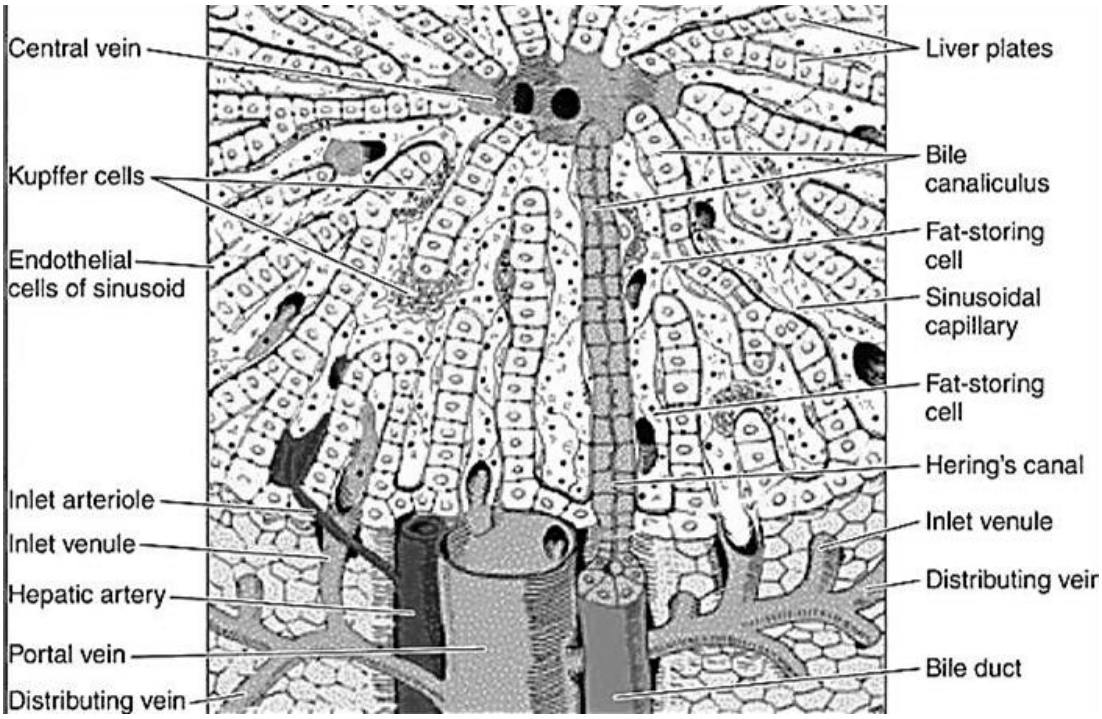


Figure.108. Diagram of a “classic” liver lobule. 1 - central vein, 2 - portal triad: a - interlobular artery, b - interlobular vein, c - interlobular bile duct, 3 - hepatic cords, 4 - hepatic sinusoids



The concepts of the liver lobules

I. The **classic liver lobule** is hexagonal in section. In the centre of the liver lobule there is a central vein. At the corners of the lobules there are the portal triads. The

blood flow is directed from periphery to the center, and bile - from the center to periphery (fig.109).

II. The **portal lobule** comprises of the adjoining parts of 3 classic lobules. It is triangular in shape and has at the center the portal triad and a central vein at the tip of each of its angles. The blood flow is directed from the center to periphery, and bile - from periphery to the center.

III. The **hepatic acinus** is situated in adjacent areas of two hepatic lobules. The terminal branches of the portal vein, an arterial branch and a bile ductule are in the center of the hepatic acinus. Theblood flow is directed from the center to periphery, and bile - from periphery to the center

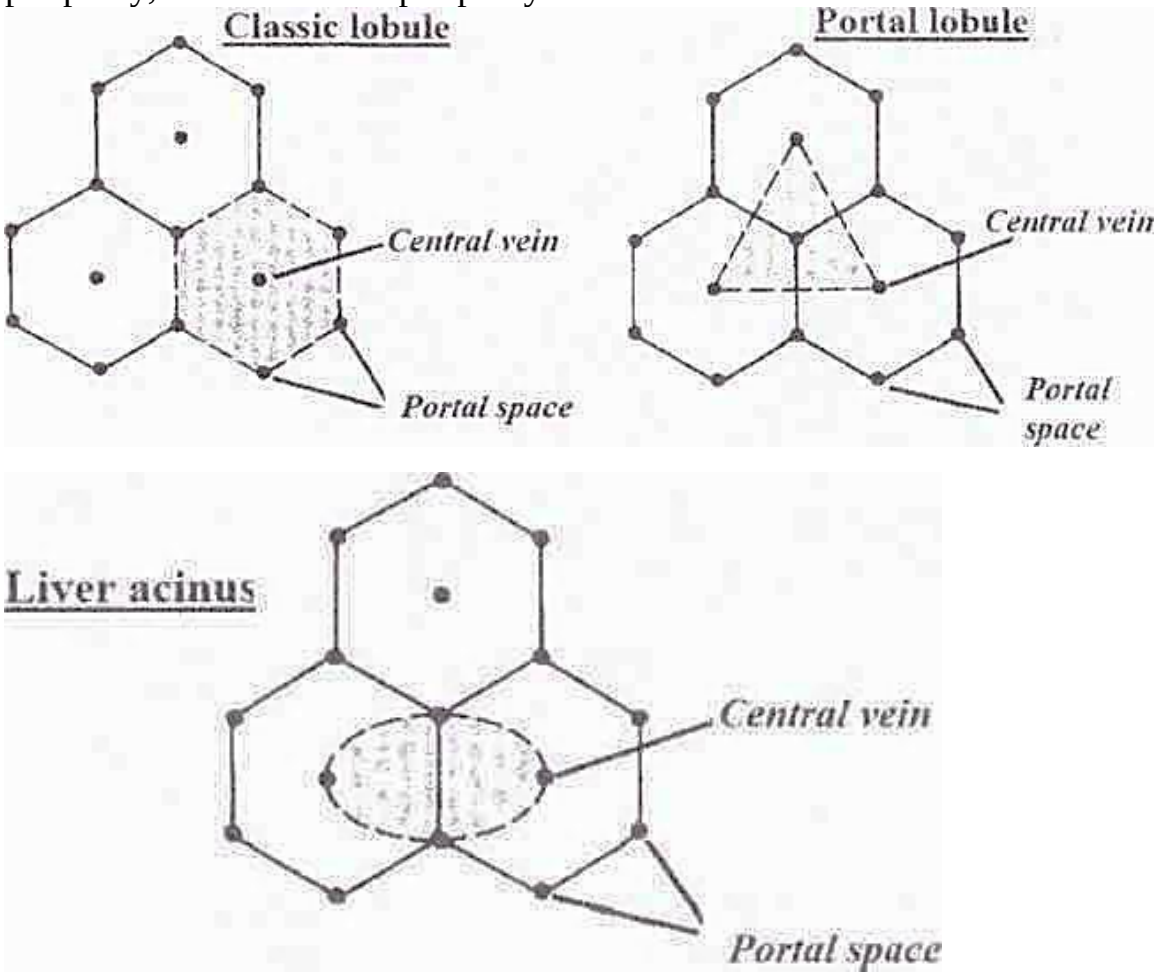


Figure 109. Schematic diagram of the liver lobules.

The endothelial cells of the wall of sinusoids are separated from the underlying hepatocytes by a narrow subendothelial space known as the perisinusoidal space (space of Disse) (fig.110). It contains the blood plasma. Microvilli of hepatocytes extend into this space, allowing proteins and other plasma components from the sinusoids to be taken up by the hepatocytes. Blood fluids percolate through the endothelial wall and make intimate contact with the hepatocyte surface, permitting an exchange of macromolecules from the sinusoidal lumen to the liver cell and vice versa.

Sinusoid lining cells:

1) endothelial cells;

2) **Kupffer cells** (macrophages) are found on the luminal surface of the endothelial cells. Kupffcr cells are typical macrophages;

3**) hepatic stellate cells (Ito cells)** are located in the spaces of Disse; they have the capacity to accumulate exogenously administered vitamin A; the stellate cell is the major cell type involved in liver fibrosis, which is the formation of scar tissue in response to liver damage;

4) **pit cells** are hepatic natural killer cells that are located in the liver sinusoids where they adhere to endothelial cells; pit cells are involved in killing metastasizing tumor cells.

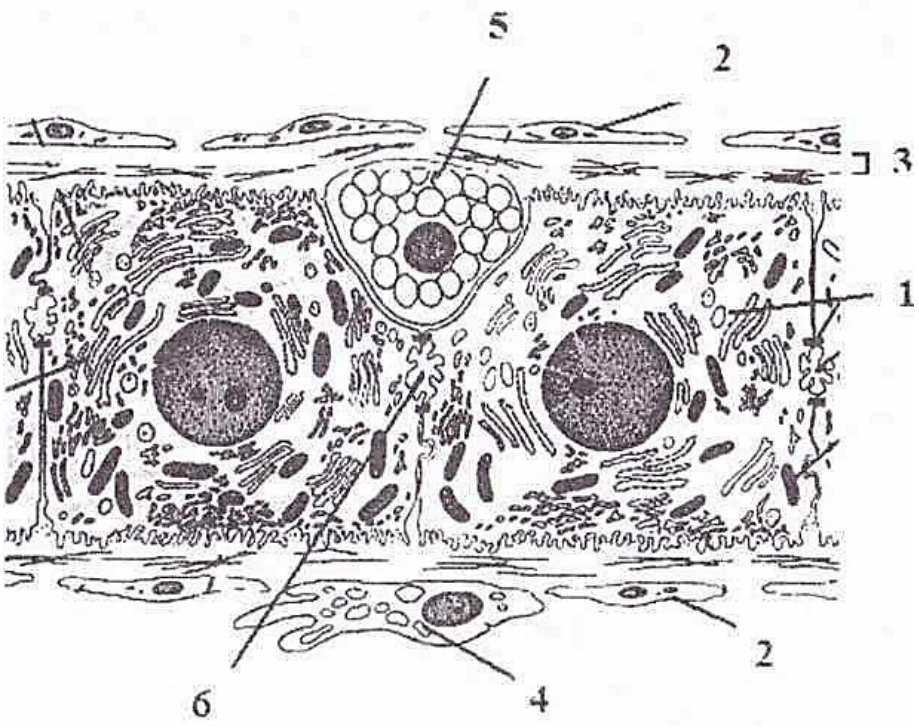


Figure 110. Schematic diagram of space of Disse. 1 - hepatocyte, 2 - endothelium of sinusoids, 3 - space of Disse, 4 - Kupffer cell, 5 - Ito cell, 6 - bile canaliculus

Hepatocytes. The hepatocytes are large polygonal cells (fig.111). The liver cell has one or two rounded nuclei with dispersed chromatin and prominent nucleoli. Some of the nuclei are polyploid; most cells in the adult are tetraploid (4n amount of DNA)

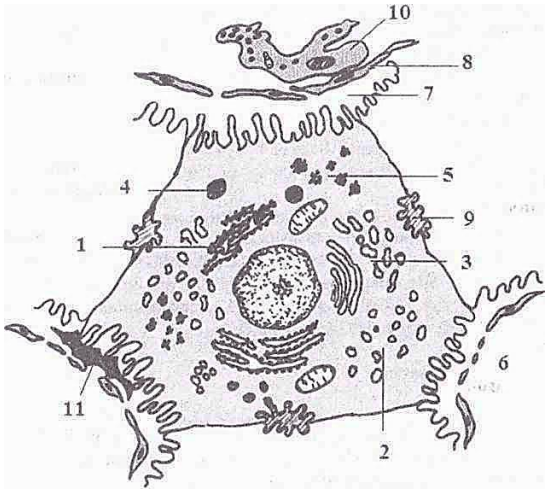


Figure 111. Schematic diagram of hepatocyte. 1 - rough endoplasmic reticulum, 2 - smooth endoplasmic reticulum, 3 - Golgi complex, 4 — lysosome, 5 - glycogen, 6 — hepatic sinusoid, 7 — space of Disse, 8 - sinusoidal endothelium, 9 - bile canaliculus, 10 - Kupffer cell, 11 - Ito cell

The hepatocytes have abundant endoplasmic reticulum - both smooth and rough. The rough endoplasmic reticulum forms aggregates in the cytoplasm. Several proteins are synthesized on polyribosomes in these structures. The smooth endoplasmic reticulum is responsible for the processes of oxidation, methylation. and conjugation required for inactivation or detoxification of various substances. Each liver cell has approximately 2000 mitochondria.

Hepatocyte **lysosomes** are responsible for degradation of intracellular organelles and endocytosis of many macromolecules. **Peroxisomes** are abundant in hepatocytes. The functions **of Golgi complexes** include the formation of lysosomes and secretion of plasma proteins. Zonal features of the hepatocytes The surface of each liver cell is in contact with the wall of the sinusoids, through the **space of Disse,** and with the surfaces of other hepatocytes.

1) The surface of the hepatocyte that feces the space of Disse has many microvilli protruding in that space.

2) Wherever two hepatocytes abut, they delimit a tubular space between - the bile canaliculus. The canaliculi are limited only by the plasma membranes of two hepatocytes. The cell membranes near these canaliculi are firmly joined by tight junctions.

Biliary system. The biliary system is the system of canals on which bile from a liver flows to the gallbladder and than to the duodenum. Biliary tract includes intrahepatic and extrahepatic passages. **Intrahepatic passages consist of:**

- intralobular (the bile canaliculi and the bile ductules) and
- interlobular are situated in the interlobular connective tissue (the bile ducts).

Extrahepatic passages consist of:

- right and left hepatic ducts,
- hepatic duct,
- common bile duct (ductus choledochus).

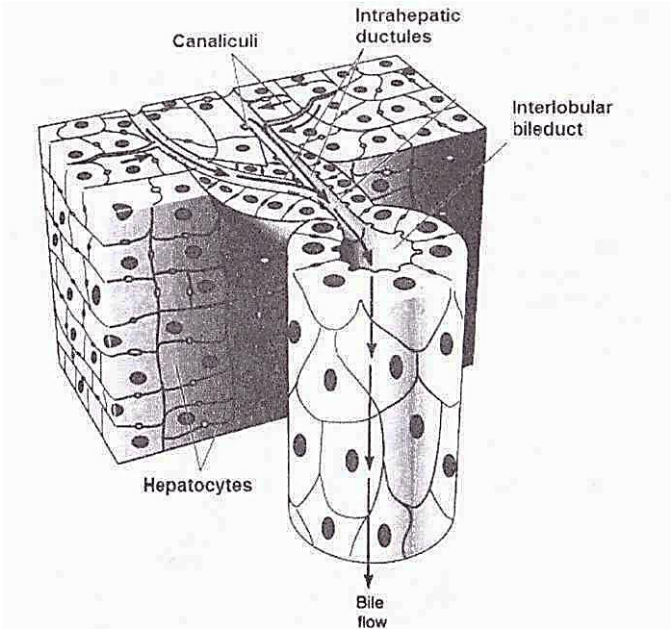
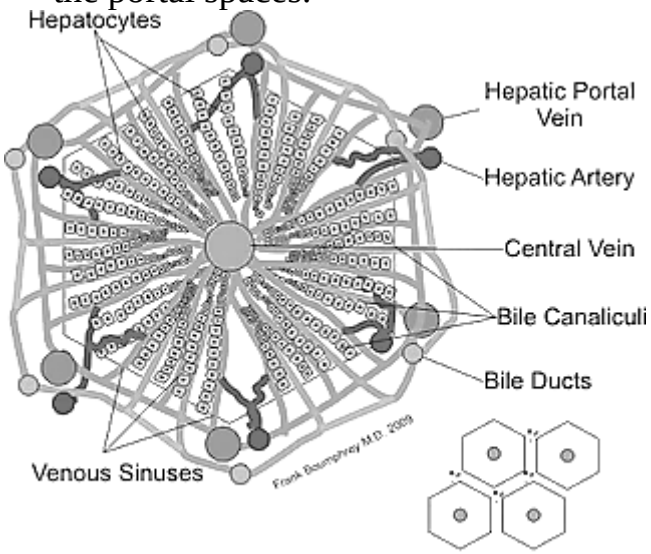


Figure 112. The bile canaliculi.

The bile canaliculi (fig.112) are thin tubes that collect bile secreted by hepatocytes. The bile canaliculi are formed by grooves on the lateral faces of the hepatocytes. The bile canaliculi form a complex anastomosing network progressing along the cords of the liver lobule and terminating in the region of the portal spaces.



Basic Structure of Liver Lobule

The bile flows from the center of the classic lobule to its periphery. At the periphery, bile enters the intrahepatic bile ductules, or Herings canals. After a short distance, the ductules cross the limiting hepatocytes of the lobule and end in the interlobular bile ducts in the portal triads. They gradually enlarge and fuse, forming right and left hepatic ducts, which leave the liver. Intrahepatic bile ductules are lined by a cuboidal epithelium. All other parts of the bilary system are lined by a tall columnar epithelium

Gallbladder The gall bladder is a pear-shaped sac that stores and concentrates bile (30-70 mL). The wall of the gall bladder consists of 3 layers (fig.113):

I. **Mucosa** has numerous branching and anastomosing folds and consists of:
1). epithelium is simple columnar specialized for absorption, with an apical brush border of microvilli; gall bladder epithelium includes only this single cell type; it has no goblet cells;
2). lamina propria is formed by loose connective tissue.

II. **Fibro-muscular layer** contains smooth muscle tissue and loose connective tissue.

III. **Adventitia** covers the upper surfaces of the body and neck; the fundus and lower surface of the body have a serous layer. Mucosa forms deep diverticula, called Rokitansky-Ashoff sinuses. Bacteria may accumulate in these sinuses, causing chronic inflammation

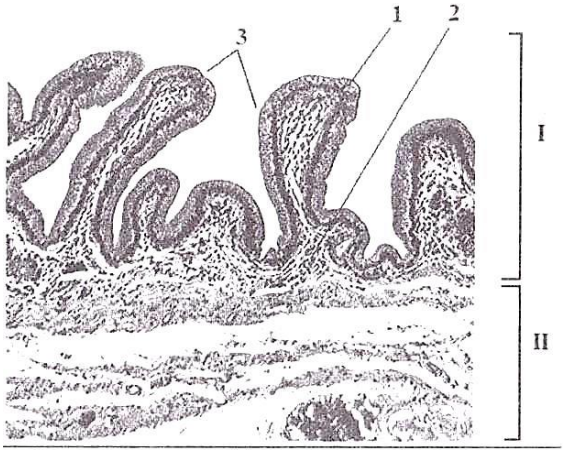
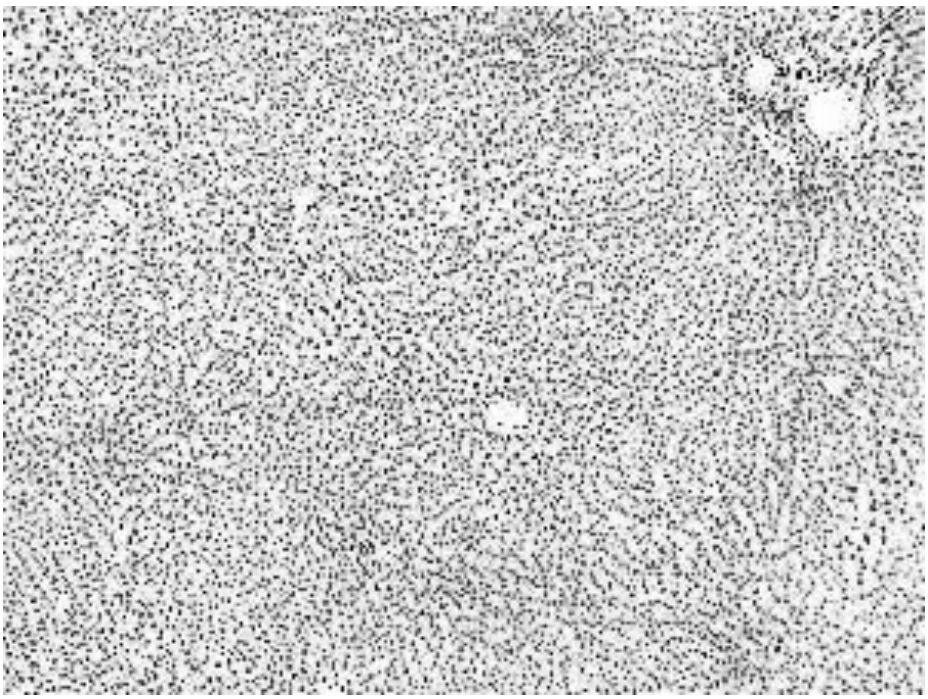


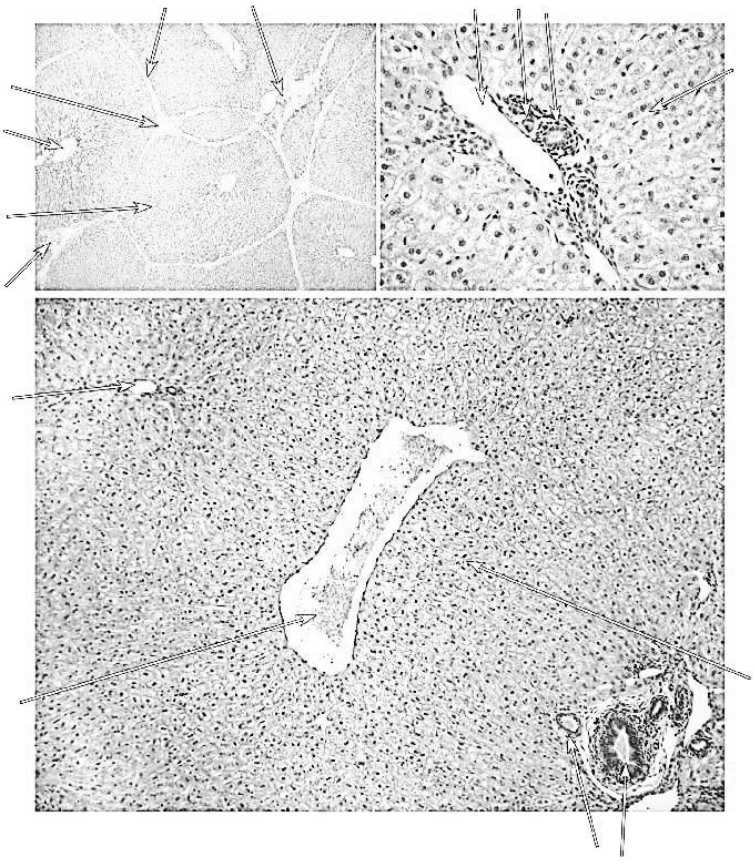
Figure 113. Photomicrograph of gallbladder structure. I- mucosa, 1 - epithelium, 2 - lamina propria, 3 - mucosal folds, II - fibro-muscular layer

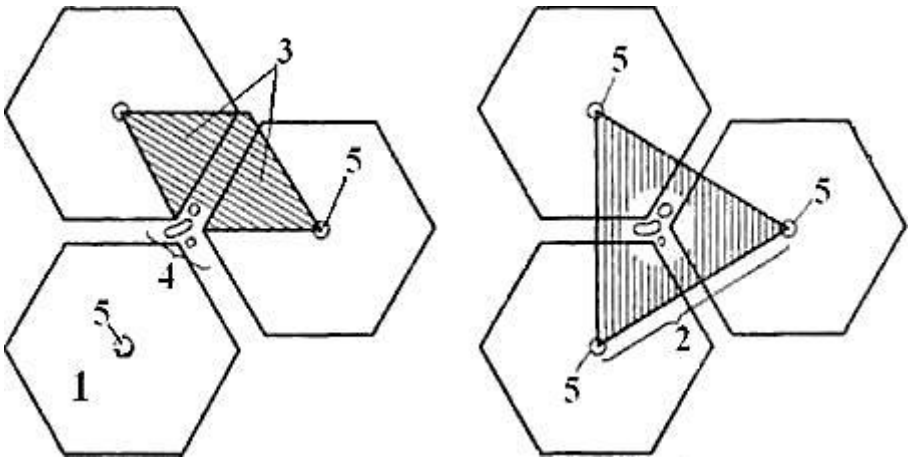
Practical lessons

1. Liver. Morphofunctional characteristic. Peculiarities of the blood supply.
2. Structure of classic hepatic lobule. Intralobular hemocapillary. Hepatic cords. Hepatocytes (structure and functions).
3. The terms: “hepatic acinus” and “portal lobule”. Bile ducts. Gallbladder: structure and functions.
4. Pancreas. Structure and functions of the exocrine portion.
5. Pancreas. Structure and functions of the endocrine portion.
6. Pancreatic acinocytes: structural peculiarities. Structure of excretory ducts.
7. Cell types of the pancreatic islands, their morphofunctional characteristic.

Paint and mark basic histological structure



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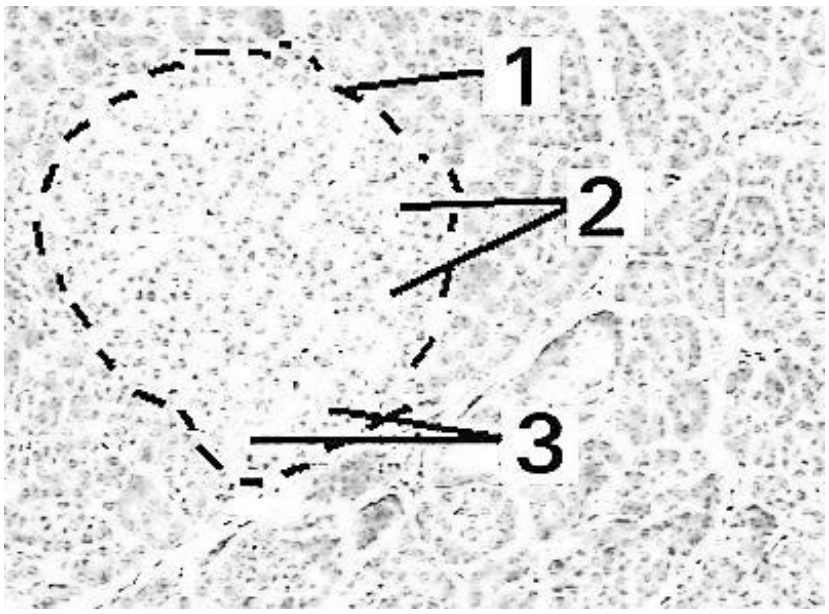
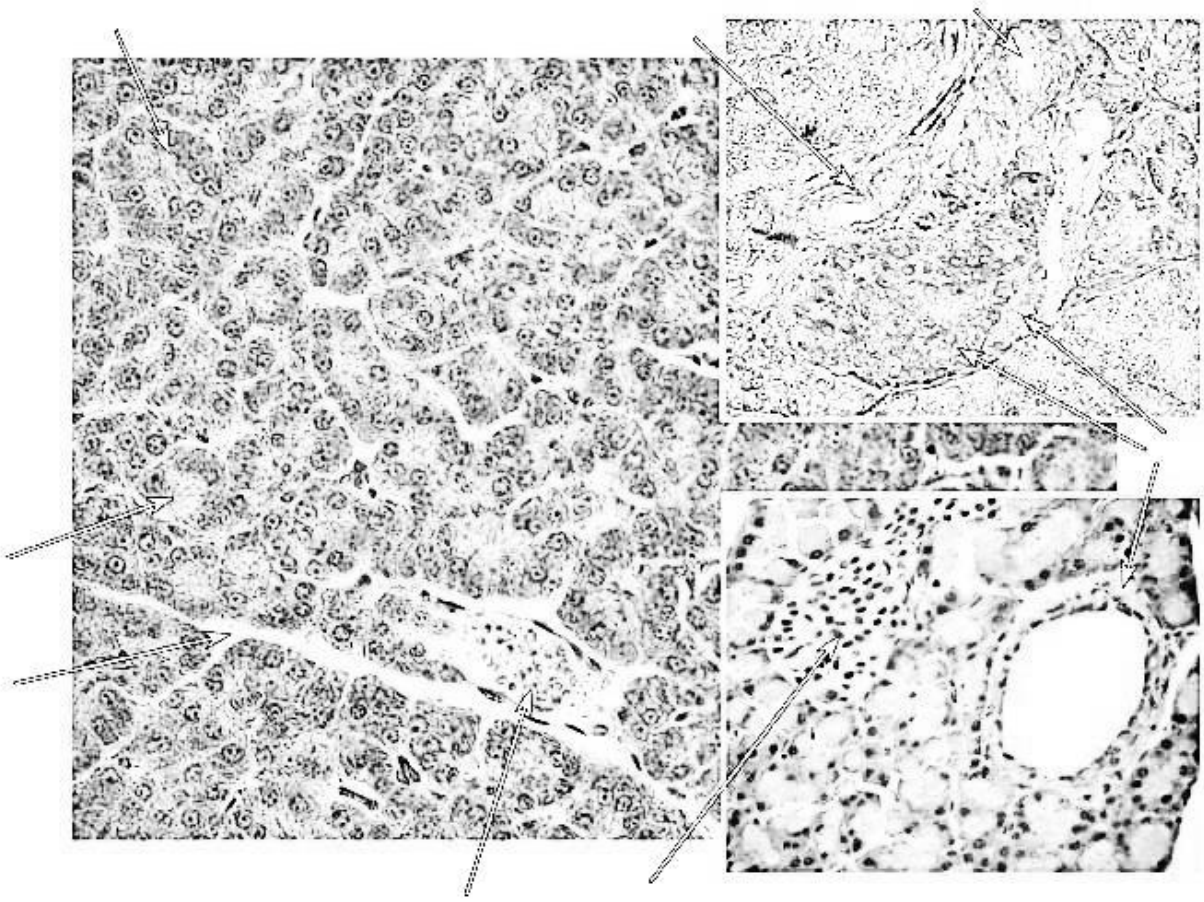




Signature of teacher_____

RESPIRATORY SYSTEM

Overview of the respiratory system. The respiratory system includes the lungs, series of air passages that link the sites of gas exchange with the external environment and the respiratory' muscles.

Functions of the respiratory system are:

1) respiration (gas exchange);
2) conditioning of the air (warming, moistening, removal of particulate materials);
3) vocalization (when the air passes through the pharynx and larynx, it makes the vocal cords in larynx to vibrate which helps in production of sound and speech in humans);
4) sense of smell (olfactory mucosa of the nasal cavity);
5) endocrine functions (hormone production and secretion of prostaglandins, angiotensin I);
6) coughing and sneezing (when any foreign particles enter the nasal passages, it can result into irritation; these irritants are forced out of the respiratory tract through cough or even sneeze);
7) protective (airway epithelial cells can secrete a variety of molecules that aid in lung defense: secretory immunoglobulins (IgA), collectins (including surfactant), and other peptides; these secretions can act directly as antimicrobials to help keep the airway free of infection);
8) fibrinolysis (lungs contain a fibrinolytic system that lyses clots in the pulmonary vessels).

The respiratory system is divided into two principal regions:

- **conducting portion**, consisting of • nasal cavity, • nasopharynx, ® larynx, • trachea, • bronchi, • bronchioles, and • terminal bronchioles. The conducting portion serves two main functions:
  - to provide a conduit through which air can travel to and from the lungs;
  - to conditioning the inspired air; and
- **respiratory portio**n, consisting of • respiratory bronchioles, • alveolar ducts, • alveolar sacs, and • alveoli. The function of respiratory portion is the exchange of oxygen and carbon dioxide between inspired air and blood.

Conducting portion .The **wall of the conducting portion** of the respiratory system consists of:

I. mucosa.

1) respiratory epithelium - pseudostratified columnar ciliated (simple cuboidal in the smallest airways);
2) lamina propria consists of loose connective tissue, contains lymphoid aggregations; these form part of the mucosa-associated lymphoid tissue, which secrete Ig A as a defense against invading microorganisms;
3) muscularis mucosa consists of smooth muscle tissue, becomes increasingly prominent as the airway diameter decreases;

II. submucosa consists of loose connective tissue, contains serous and mucous glands which become less numerous in the narrow airways and are not present beyond the tertiary bronchi;

III.fibro-cartilage layer diminishes as the diameter of the airway decreases to be absent beyond the tertiary bronchi;

IV. **adventitia consists** of loose connective tissue.

Respiratory epithelium consists of' **five cell types** (fig, 114):

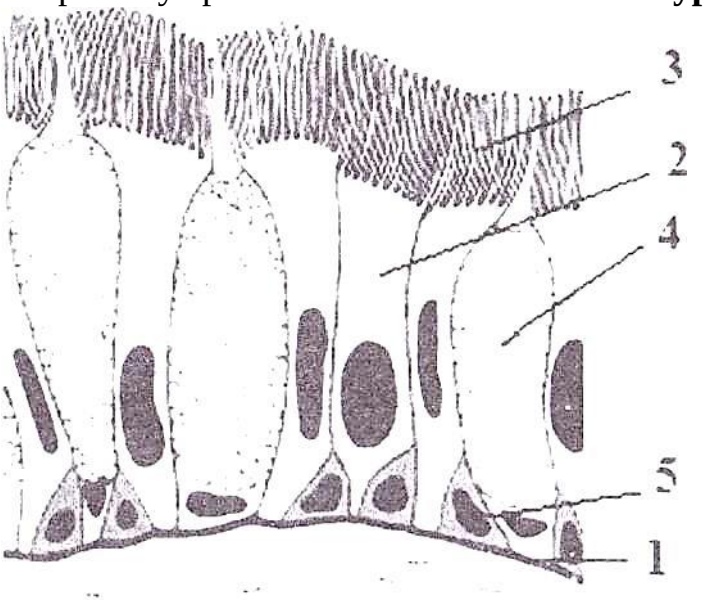


Figure 114. Schematic diagram of the respiratory epithelium. 1 - basal lamina, 2 - ciliated columnar cell, 3 - cilia, 4 - goblet cell, 5 - basal cell

1.**ciliated columnar cells** constitute the most abundant type; they have about 300 cilia on its apical surface;

2**. mucous goblet cells** have mucous droplets on their apical portion;

3. **brush cells** have numerous microvilli on their apical surface. The basal surface of these cells is in contact with afferent nerve endings. Thus, the brush cells are regarded as a receptor cells;

4. **basal (short**) cells are small rounded cells that lie on the basal lamina; they differentiate into the other cell types;

5**. small granule cells** have numerous granules; these cells constitute a population of cells of the diffuse neuroendocrine system. Vestibule is lined by stratified squamous epithelium, contains numerous hairs, sebaceous and sweat glands Respiratory region is lined by pseudostratified columnar ciliated epithelium with numerous goblet cells; the lamina propria is very vascular, which serves to warm the inspired air; it contains serous and mucous glands. Paranasal sinuses are lined by pseudostratified columnar ciliated epithelium with few goblet cells.

Trachea

The trachea has 4 layers (fig. 115):

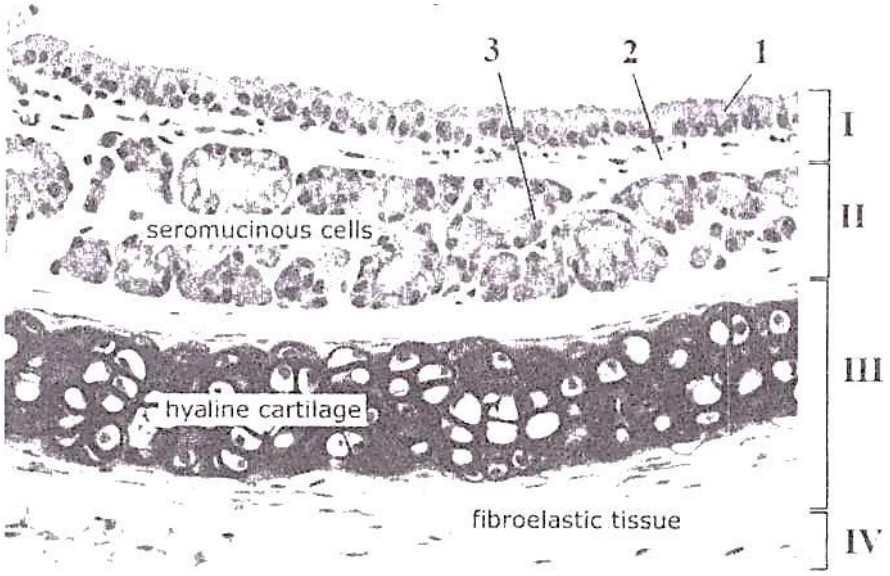


Figure 115. Photomicrograph of trachea. I - mucosa: 1 - respiratory epithelium, 2 - lamina propria; II - submucosa: 3 - secretory portions of gland; III - fibro-cartilage layer; IV – adventitia

I. **mucosa** 1) respiratory epithelium is pseudostratified columnar ciliated; 2) lamina propria consists of loose connective tissue with elastic fibers, contains mucous, serous and mixed glands;
II. **submucosa** consists of loose connective tissue, contains serous and mucous glands;
III. **fibro-cartilage** layer contains 16-20 hyaline C-shaped rings; the posterior ends of the cartilages are connected by connective tissue and smooth muscle; IV. adventitia consists of loose connective tissue.

Bronchial tree(fig. 116)**.** The trachea divides into 2 primary bronchi that enter the lungs at the hilum. After entering the lungs, the primary bronchi give rise to three bronchi in the right lung and two in the left lung, each of which supplies a pulmonary lobe. These lobar bronchi divide repeatedly, giving rise to smaller bronchi, whose terminal branches are called bronchioles. Each bronchiole enters a pulmonary lobule, where it branches to form 5-7 terminal bronchioles. Histologically bronchi are divided into large, middle and small. The wall of bronchi has features in each part of a bronchial tree.

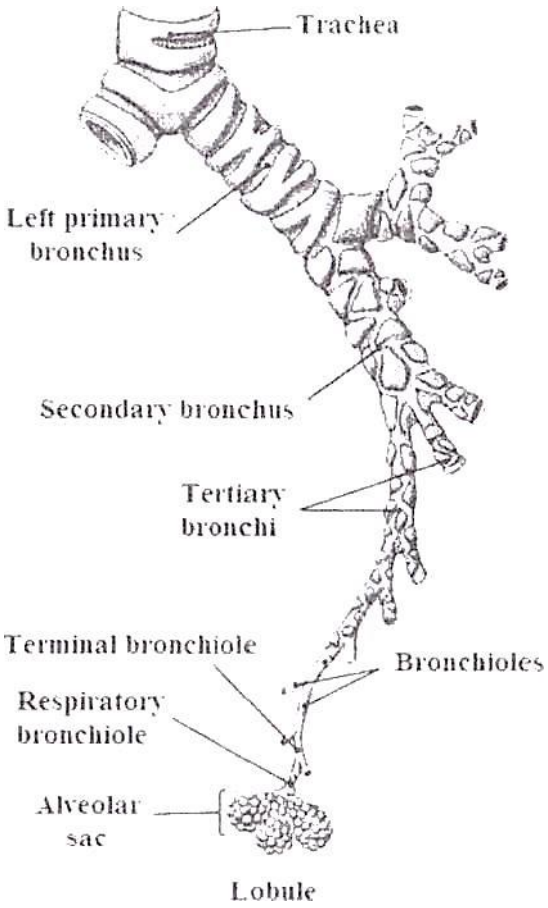


Figure 116.. Schematic diagram of the bronchial tree

Main (primary) bronchi (diameter 15 mm) have the same structure as a trachea.

I.Mucosa

1) ***respiratory epithelium*** is pseudostratified columnar ciliated;

2***) lamina propria*** consists of loose connective tissue with elastic fibers, contains mucous, serous and mixed glands;

3) ***muscularis mucosa*** formed circular and slanting smooth myocytes.

II. submucosa consists of loose connective tissue, contains serous and mucous glands;

III. fibro-cartilage layer contains solid rings of hyaline cartilage.

IV. **adventitia** consists of loose connective tissue.

Large bronchi (diameter 10-15 mm) (lobar or secondary, segmental or tertiary).

I. Mucosa

1) ***respiratory epithelium*** is pseudostratified columnar ciliated with numerous goblet cells;

2***) lamina propria*** consists of loose connective tissue with elastic fibers, contains numerous mucous, serous and mixed glands;

3) ***muscularis mucosa*** mucosa forms closed rings, consists of circular and slanting smooth myocytes.

II. submucosa consists of loose connective tissue, contains serous and mucous glands;

III. fibro-cartilage layer contains of hyaline the cartilage rings are replaced by isolated plates

IV. adventitia consists of loose connective tissue.

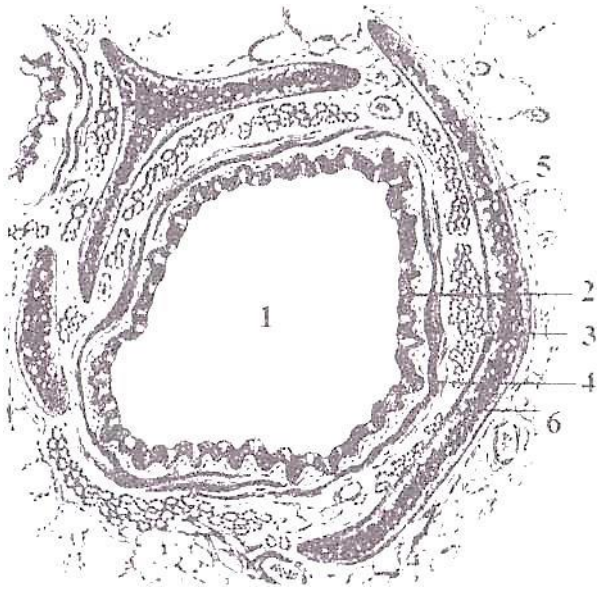


Figure 117.Large bronchus. 1 - lumen 2 - pseudostratified columnar ciliated epithelium, 3 - lamina propria, 4 - muscularis mucosa, 5 - glands, 6 - hyaline cartilage.

Middle bronchi (diameter 5-2 mm) (subsegmental) are covered by pseudostratified columnar epithelium which is lower, than in large, with the smaller content of goblet cells; a smooth muscle cells form crisscrossing bundles; glands are few, fibrocartilage layer contains the islands of an elastic cartilage. Small bronchi (diameter 2 mm or less) (intralobular) (fig. 118) are covered by lower epithelium, than middle, goblet cells are individual; glands and cartilage are absent, a smooth muscle cells form circular bundles. Smooth muscle tone controls the diameter of the conducting passages. Terminal bronchioles are more distal part of the conducting passages with diameter 1mm or less. They are lined by simple cuboidal epithelium containing Clara cells. Cartilage, glands and goblet cells are absent; lamina propria contains the elastic fibers and smooth muscle cells which are spirally arranged.

Middle bronchi

I. Mucosa

1) ***respiratory epithelium*** is pseudostratified columnar ciliated which is lower;

2***) lamina propria*** consists of loose connective tissue with elastic fibers, contains mucous, serous and mixed glands, glands are few;

3) ***muscularis mucosa*** a smooth muscle cells form crisscrossing bundles.

II. submucosa consists of loose connective tissue, contains serous and mucous glands;

III. fibro-cartilage layer contains contains the islands of an elastic cartilage.

IV. <u>adventitia</u> consists of loose connective tissue.

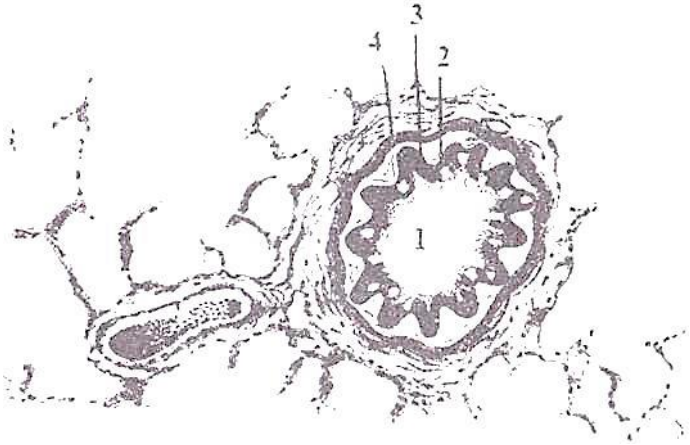


Figure 118. Small bronchus. 1 - lumen, 2 - pseudostratified ciliated epithelium, 3 — lamina propria, 4 — muscularis mucosa.

Small bronchi (diameter 2 mm or less)

I. <u>Mucosa</u>

1) ***respiratory epithelium*** is pseudostratified columnar ciliated covered by lower epithelium, than middle, goblet cells are individual;

2***) lamina propria*** consists of thin layer loose connective tissue, **glands are absent**,

3) ***muscularis mucosa*** mucosa forms closed rings, consists of circular and slanting smooth myocytes. Smooth muscle tone controls the diameter of the conducting passages: by circular muscles narrowed bronchial lumen and circular muscles reduce the length of the bronchus.

II. <u>submucosa</u> consists of loose connective tissue, contains serous and mucous glands;

III. <u>fibro-cartilage</u> layer **are absent**.

IV. <u>adventitia</u> consists of thin layer loose connective tissue.

Terminal bronchioles are more distal part of the conducting passages with diameter 1mm or less. They are lined by simple cuboidal epithelium containing Clara cells. Cartilage, glands and goblet cells are absent; lamina propria contains the elastic fibers and smooth muscle cells which are spirally arranged.

Clara cells (nonciliated bronchiolar secretory cells) are domeshaped cells with short microvilli found in the small airways (bronchioles) of the lungs. These cells may secrete glycosaminoglycans to protect the bronchiole lining. One of the main functions of Clara cells is to protect the bronchiolar epithelium. They do this by secreting a small variety of products, including Clara cell secretory protein (CCSP) and a solution similar to the component of the lung surfactant. They are also responsible for detoxifying harmful substances inhaled into the lungs.

Respiratory portion of the respiratory system. The respiratory portion of the respiratory system consists of structural and functional units - **acini** - each includes respiratory bronchioles, alveolar ducts and alveolar sacs (fig. 119). Acini

separate by thin layers of loose connecting tissue; 12-18 acini form pulmonary lobule.

Respiratory bronchioles. Each terminal bronchiole subdivides into 2 respiratory bronchioles. The respiratory bronchiolar structure is identical to that of the terminal bronchioles. But the wall of respiratory bronchiole is beset with a number of alveoli, where gas exchange occurs. **Alveolar ducts.** Each respiratory bronchiole divides into alveolar ducts. They are lined by squamous epithelium.

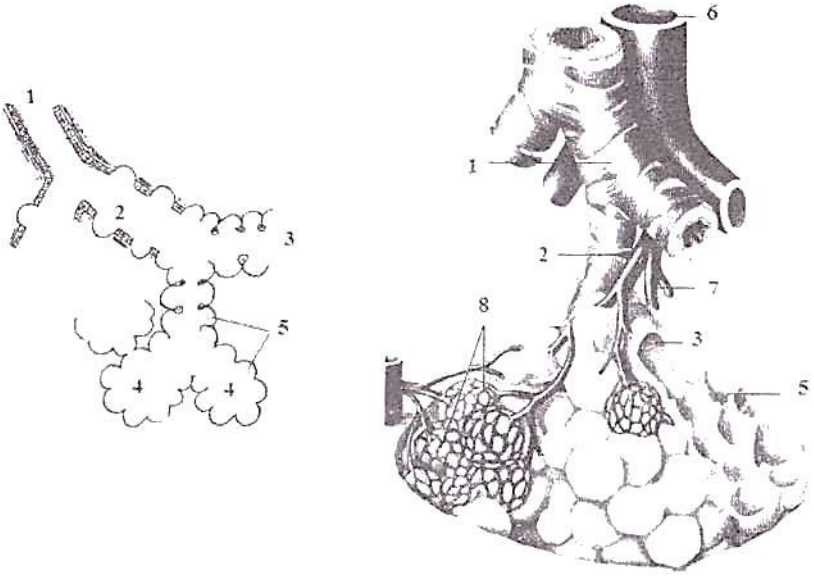


Figure 119. Schematic diagrams of the terminal bronchiole and acinus of the lung. 1 — terminal bronchiole, 2 — respiratory bronchiole, 3 — alveolar duct, 4 — alveolar sacs, 5 - alveoli, 6 - branch of pulmonary artery, 7 - arteriole, 8 - capillaries

In the lamina propria surrounding the rim of the alveoli is a network of smooth muscle cells. The smooth muscle of the respiratory bronchioles and alveolar ducts regulates alveolar air movements. Smooth muscle disappears at the distal ends of alveolar ducts. Alveolar ducts open into atria that communicate with alveolar sacs. Each of alveolar ducts gives rise to several alveoli. Alveoli Alveoli are saclike evaginations of the respiratory bronchioles, alveolar ducts, and alveolar sacs. Alveoli are densely packed together; inter-alveolar septa form a common wall between adjacent alveoli. These septa contain network of elastic fibers and blood vessels. Neighbouring alveoli may be connected to each other by small alveolar (Kohn')pores (fig. 120).

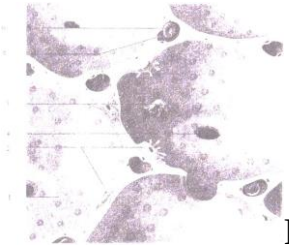


Figure 120. Schematic diagram of pulmonary alveoii. 1 - type I cell, 2 - type II cell, 3 - alveolar macrophage, 4 - alveolar pore, 5 - capillaries, 6 - erythrocyte

Alveoli are lined by simple squamous epithelium. Alveolar epithelium consists of cells of two types:

type I cell (squamous alveolar cell) are flattened, irregularshaped, make up 97% of the alveolar surface. They are the component of air- blood barrier;

type II cells (great alveolar cells) are rounded in shape, occupy 3% of the alveolar surface area. These cells are typical secretory cells; they secrete a surface-active lipoprotein complex (phospholipoprotein) called surfactant. Surfactant reduces surface tension and prevents alveoli from collapsing during expiration. Brush cells are also present in the alveolar wall, but they are few in number. They may serve as receptors that monitor air quality in the lung.

Alveolar macrophages or dust cells are found in the alveolar wall or free in the alveolar space. They are derived from blood monocytes.

Air-blood barrier (Fig.121). Air in the alveoli is separated from capillary blood by components, which form the air-blood harrier (fig. 121). The air-blood barrier exists in the gas exchanging region of the lungs. It exists to prevent air bubbles from forming in the blood, and from blood entering the alveoli.

The air-blood barrier is formed by:

1) cytoplasm of type 1 cells;
2) fused basal laminae of the alveolar and endothelial cells;
3) cytoplasm of endothelial cells.

The barrier is permeable to molecular oxygen, carbon dioxide, carbon monoxide and many other gases.

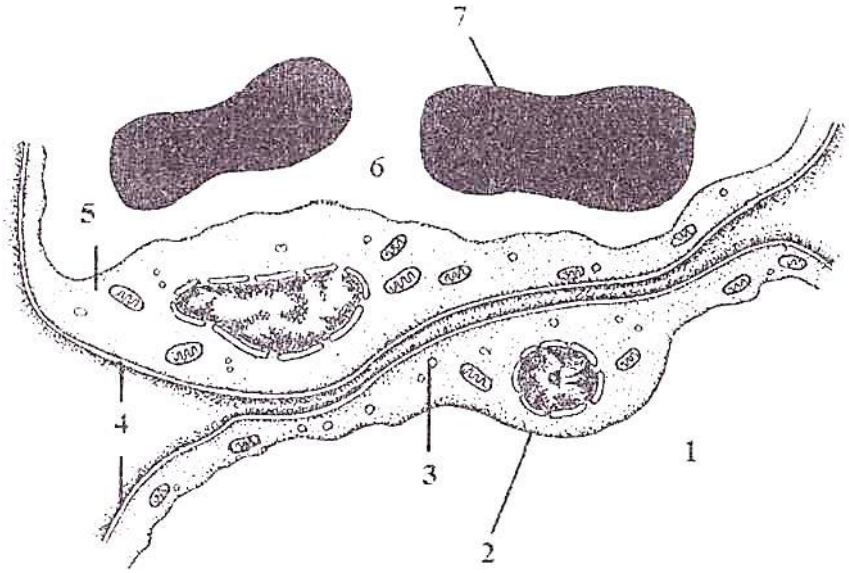


Figure 121. Schematic diagram of the air-blood barrier. 1 - alveole, 2 - surfactant, 3 - type I cell, 4 - fused basal laminae, 5 - endothelial cell, 6 - capillary, 7 - erythrocytes

Pleura. The pleura is a serous membrane which folds back onto itself to form a twolayered, membrane structure.

The thin space between the two pleural layers is known as the pleural cavity; it normally contains a small amount of pleural fluid. The **outer pleura** (parietal pleura) is attached to the chest wall. **The inner pleura** (visceral pleura) covers the

lungs and adjoining structures. Pleura is formed by mesothelial cells overlying vascularised loose connective tissue. The parietal pleura is highly sensitive to pain while the visceral pleura is not, due to its lack of sensory innervation. **Development of the respiratory system**.Upper part of respiratory system (from nose to larynx) develops from the pharyngeal apparatus which is a part of head and neck. Lower part of respiratory system (below the larynx up to lung alveoli) develops from a ventral evagination of the foregut (laryngotracheal diverticulum) (fig. 122).

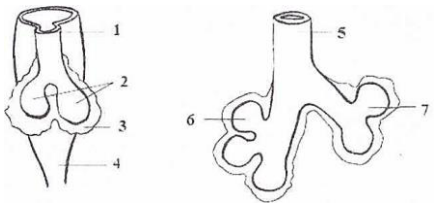


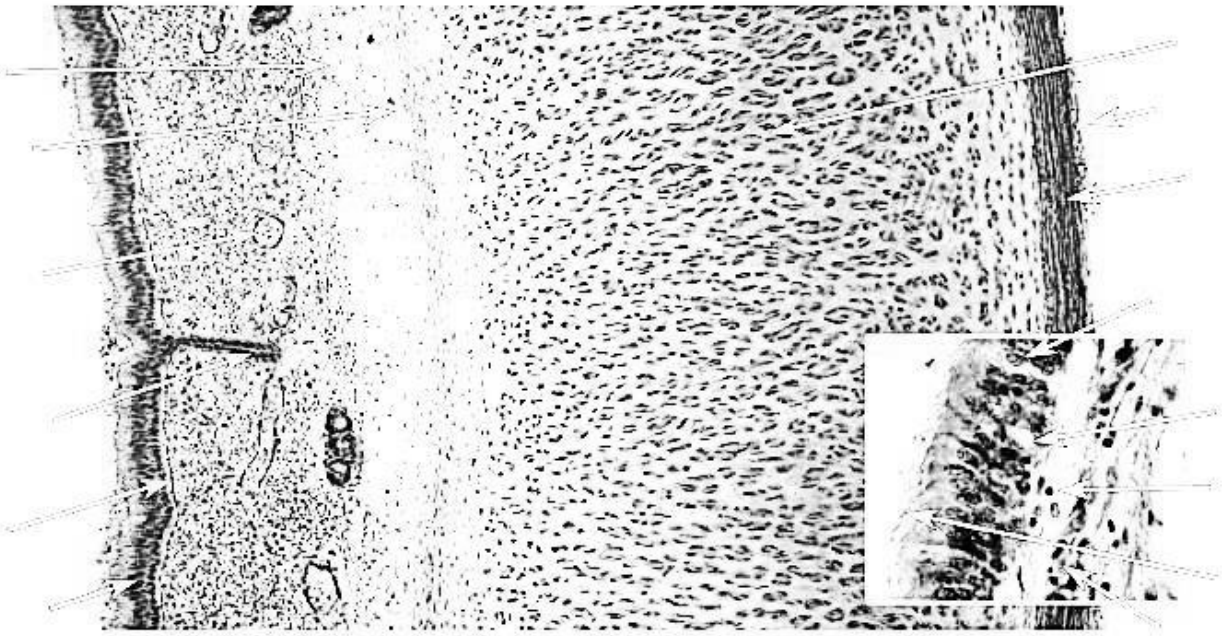
Figure 122. Stages in the development of the bronchi and lungs. 1 - laryngotracheal fold and groove, 2 - lung buds, 3 — mesenchyme, 4 - esophagus, 5 - trachea, 6 — right lobar bronchi, 7 - left lobar bronchi

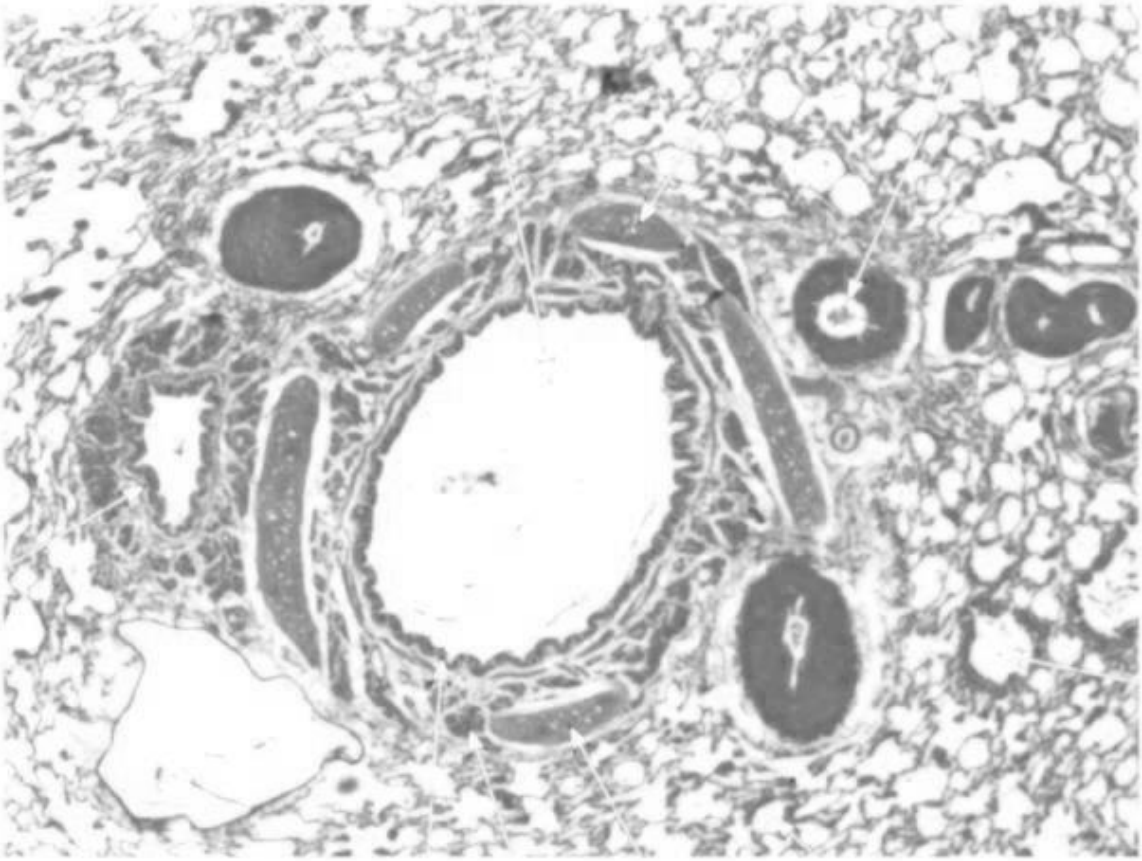
The laryngotracheal diverticulum arises from endoderm on the ventral wall of the foregut. Tracheoesophageal folds develop on either side and join to form a tracheoesophageal septum that separates it from the rest of the foregut. This divides the foregut into the laryngotracheal tube (ventral) and the esophagus (dorsal). The caudal end of the laryngotracheal diverticulum enlarges to form the lung bud, which is surrounded by mesenchyme. After that the lung bud divides into two bronchial buds, which enlarge to form the bronchi. The bronchial buds give rise to the epithelium lining all the respiratory passages, the alveoli and the associated glands. The surrounding mesenchyme gives rise to the connective tissue, cartilage, muscle and blood vessels.

Practical lessons.

1.Respiratory system: general morphofunctional characteristic.
2. Conducting system. Nasal cavity, larynx, trachea: structure and functions.
3. Lungs. Bronchial tree. Peculiarities of the bronchial wall due to the calibre. Characteristic features of the epithelium conducting system.
4. Lungs: respiratory portion. Structure and functions of the acinus – lung's morphofunctional unite.
5. Microscopic structure of the lung's alveolar wall. Ultrastructure of aerohematic barrier. Conception about alveolar surfactant complex
6. Lungs: peculiarities of the blood supply.

Paint and mark basic histological structure





Signature of teacher_____

URINARY SYSTEM

Overview of the urinary system. The urinary system consists of the paired kidneys and ureters, and unpaired bladder and urethra.

Functions of the urinary system

- Regulation of water, inorganic ion balance, and acid-base balance.
- Removal of metabolic waste products from the blood and their excretion in the urine.
- Removal of foreign chemicals from the blood and their excretion in urine > Production of hormones/enzymes: 9 erythropoietin, which controls erythrocyte production; ® renin, an enzyme that controls blood pressure and blood volume; renin cleaves circulating angiotensinogen to release angiotensin I.

Kidneys The kidney (fig.123) is covered by a capsule of connective tissue consisting of collagen, elastic fibers and smooth muscle cells. **The kidney is divided into:**

- an inner medulla and
- an outer cortex.

The medulla consists of 10-18 medullary pyramids. From the base of each medullary pyramid the

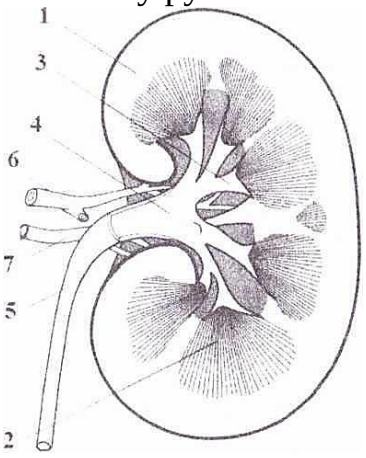


Figure 123. Schematic diagram of the kidney structure. 1 - cortex, 2 - medulla, 3 - calyx, 4 - renal pelvis, 5 - ureter, 6 - renal artery, 7 - renal vein.

medullary rays penetrate the cortex. The cortex is the peripheral part lying between the capsule and the bases of renal pyramids. The cortical tissue surrounding each medullary pyramid is a renal lobe, and each medullary ray forms the center of a conical renal lobule. A part of cortex projects inwards between the renal pyramids and forms the renal columns of Berlin.

Nephron. Each kidney is composed of 1-4 millions nephrons - the structural and functional units (fig.124).

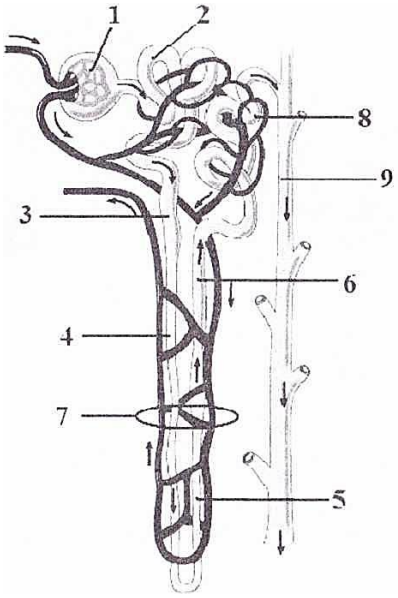
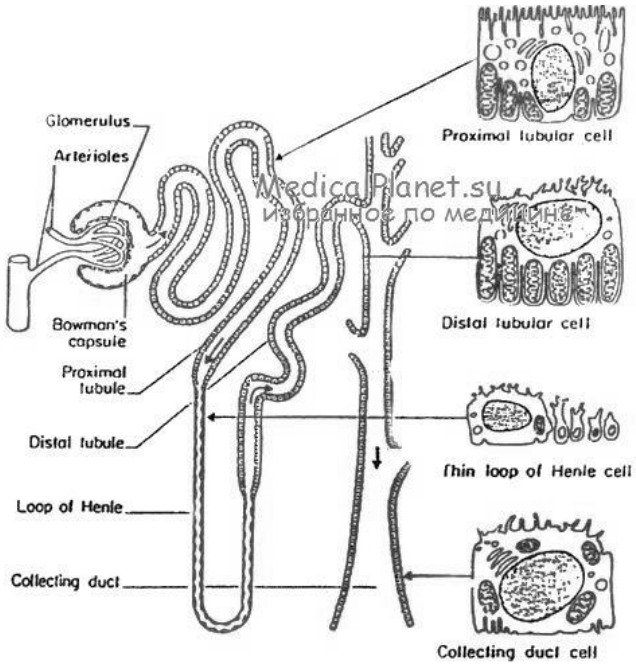


Figure 124. Diagram of the nephron structure. 1 — renal corpuscle, 2 - proximal convoluted tubule, 3 - proximal straight tubule (thick descending limb), 4 - thin descending limb of the loop of Henle, 5 - thin ascending limb of the loop of Henle, 6 - distal straight tubule (thick ascending limbs of the loop of Henle), 7 - Henle's loop, 8 - distal convoluted tubule, 9 — collecting tubule

Each nephron consists of:

1) dilated portion, the capsule of the renal corpuscle,
2) proximal convoluted tubule,
3) proximal straight tubule (thick descending limb of Henle's loop),
4) thin descending limb of Henle's loop,
5) thin ascending limb of Henle's loop,
6) distal straight tubule (thick ascending limbs of Henle's loop),
7) distal convoluted tubule.



Renal corpuscle.**Each renal corpuscle consists of** (fig.125):

- a tuff offenestrated capillaries, the glomerulus, surrounded by
- a double-walled epithelial Bowman's capsuleThe parietal layer of the capsule consists of a simple squamous epithelium surrounded by basal lamina.

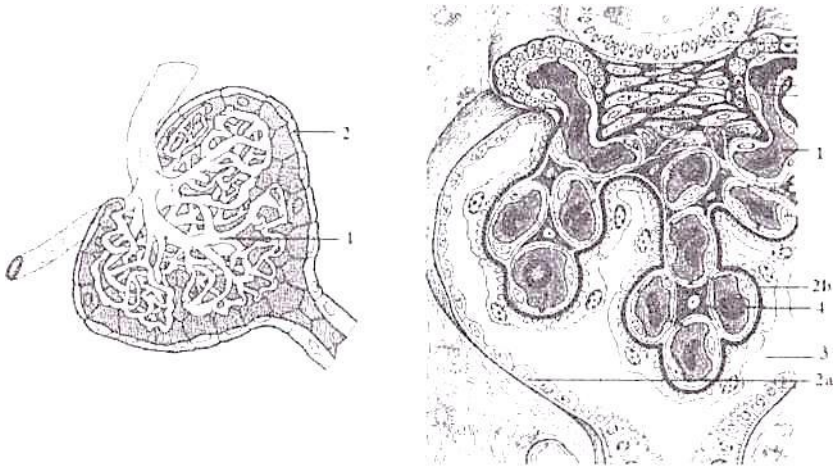


Figure 125. Diagram of the renal corpuscle structure. 1 — glomerulus, 2 - Bowman’s capsule: a - parietal layer, b - visceral layer (podocytes), 3 - urinary space, 4 - intraglomerular mesangial cell.

The visceral layer of the capsule envelops the capillaries of the glomerulus. Between two layers of Bowman’s capsule there is the urinary space, which receives the fluid filtered through the capillary wall and the visceral layer. The visceral layer lined by modified celts termed the podocytes (fig.126, 127).

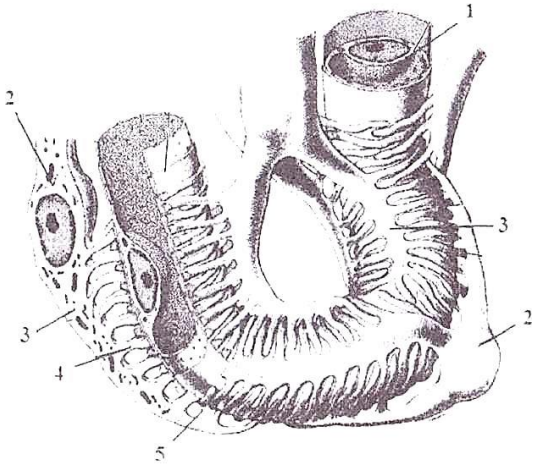


Figure 126. Visceral layer of Bowman’s capsule. 1 - blood capillary' of glomerulus, 2 — podocyte cell body, 3 - primary processes, 4 - secondary processes, 5 - filtration slits (from Jimqueira L.C., Carneiro J., 2005)

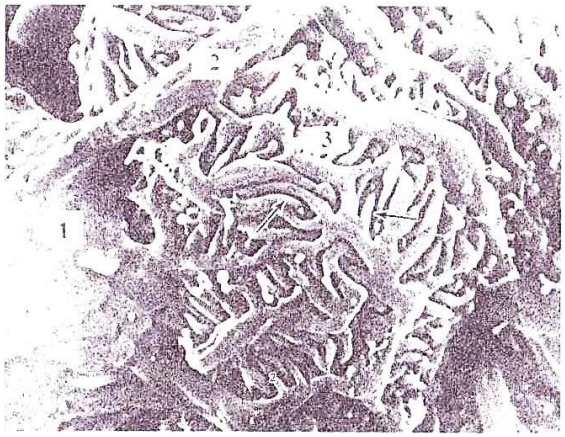


Figure 127. Scanning electron micrograph of a glomerulus. 1 - podocyte cell body, 2 - primary processes, 3 - secondary processes

The podocytes have a cell body from which several primary processes arise. Each primary process gives secondary processes, called pedicels that embrace the capillaries of the glomerulus. Between the pedicles there are little spaces termed filtration slits. Between the fenestrated endothelial cells of glomerular capillaries and the podocytes is a thick basement membrane. The basement membrane is derived from the fusion of capillary- and podocyte-produced basal laminae. Under electron microscope, one can distinguish a central electron-dense layer (lamina densa) and, on each side, a more electron-lucent layer (lamina rara). The glomerular basal lamina is a selective macromolecular filter between the blood and the glomerular filtrate. **Thus, the filtration barrier of the renal corpuscle (fig.128) consists of:**

1. cytoplasm of the fenestrated endothelial cells of glomerular capillaries;
2. thick basement membrane.
3. filtration slits between the pedicles of the podocytes.

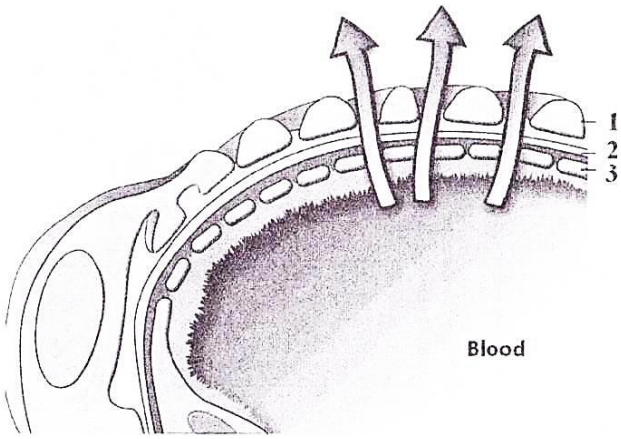


Figure 128. Schematic diagram of filtration barrier of the renal corpuscle. 1 - podocyte, 2 - basement membrane, 3- endothelial cell of glomerular capillary

Mesangium. Between capillaries there is a special tissue which consists of intraglomerular mesangial cells (fig.125). These ceils are specialized pericytes which contain contractile proteins and may act as macrophages. They are an

unusual example of phagocytic cells derived from smooth muscle and not monocytes. Tubes of the nephron (fig.129) Proximal thick segment consists of proximal convoluted tubule and proximal straight tubule (thick descending limb), and is formed by simple cuboidal or columnar epithelium. The apexes of epithelial cell have numerous microvilli, which form a brush border.

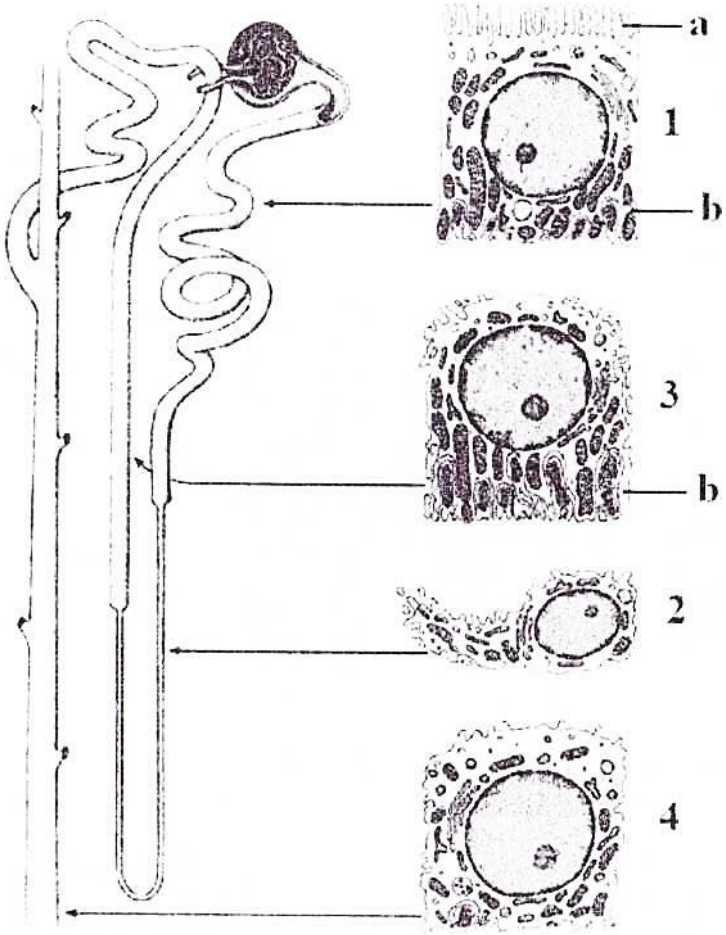


Figure 129. Diagram ot structure of the tubes of the nephron. 1 - proximal thick segment: a - brush border, b -basal striations; 2 - thin segment, 3 - distal thick segment, 4 - collecting tubule (from Junqueira L.C., CarneiroJ., 2005)

The basal portions of these cells have membrane invaginations; mitochondria are concentrated between them and arranged parallel to the long axis of the cell (basal striations).

The proximal segment is the initial and major site of reabsorption. The proximal convoluted tubules reabsorb about 150 L of fluid per day or about 80% of ultrafiltrate into the vessels of the peritubular capillary network. The proximal convoluted tubules also reabsorb amino acids, sugars, and polypeptides. Thin segment constitutes the thin part of the loop of Henle, is formed by simple columnar epithelium. Thin segment is part of the countercurrent exchange system that functions in concentrating urine.

Distal thick segment consists of distal straight tubule (thick ascending limbs of Henle's loop) and distal convoluted tubule, is lined by simple cuboidal epithelium. There is no brush border. The basal portion of these cells has basal striations Distal

straight tubule transports ions (Na+ , K+ , Cl') from tubular lumen to the interstitial connective tissue. Distal convoluted tubule is responsible for reabsorption of Na+ and secretion of K+ into ultrafiltrate, reabsorption of bicarbonate ions.

Collecting duct system The collecting duct system of the kidney consists of a series of tubules and ducts that connect the nephrons to the ureter. It participates in electrolyte and fluid balance through reabsorption and excretion, processes regulated by the hormones aldosterone and antidiuretic hormone.

The collecting duct system includes the collecting tubules, cortical collecting ducts, and medullary collecting ducts. Urine passes from the distal convoluted tubules to collecting tubules that join each other to form larger, collecting ducts, finally the papillary ducts of Bellini, which open at the apex of each renal papilla. **Collecting tubules** and collecting ducts are lined by simple cuboidal or columnar epithelium which consists of two types of cells:

- **light cells** are principal cells of this system with electron-lucent cytoplasm and few organelles; function of these cells is passive reabsorption of water;
- **dark intercalated** (IC) cells with microvillous surface and mitochondria in the cytoplasm; function of these cells is secretion of hydrochloric acid.

Types of the nephrons (fig.130)

1). **Cortical** (subcapsular) nephrons constitute 80%; their glomeruli are located high in the cortex, these nephrons have short loops. Glomeruli function under the high pressure and actively participate in formation of glomerular ultrafiltrate.

2). **Juxtamedullary** nephrons constitute 2 0%; their glomeruli are located near the corticomedullary junction, they have very long Henle's loops, extending deep into the medulla. Glomeruli function under small pressure and don't play the important role in a process of a filtration. Their structural features are essential to the urine-concentrating mechanism.

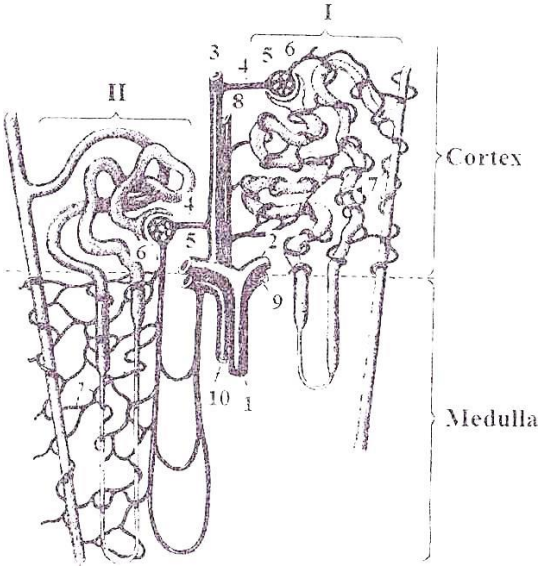


Figure 130. Kidney blood supply. I - cortical nephron, II - juxtamedullary nephrons; 1 - interlobar artery, 2 - arcuate artery, 3 - interlobular artery, 4 - afferent arteriole, 5 - capillaries of the glomerulus, 6 — efferent arteriole, 7 - peritubular capillary network, 8 - interlobular vein, 9 - arcuate vein, 1 0 - interlobar vein.

Kidney blood supply The kidney has a rich blood supply. 1200-1300 ml of blood passes through both kidneys each minute.

Arteries Kidney receives blood from renal artery, which near the hilum of the kidney gives rise to 5 segmental arteries. Each segmental artery gives off interlobar arteries (flg.130), located between the renal pyramids. At the level of the corticomedullary junction, the interlobar arteries form the arcuate arteries. Arcuate arteries give off interlobular arteries, which follow in the cortex vertically towards to the renal surface. Interlobular arteries give arise the afferent arterioles, which supply blood to the capillaries of the glomeruli (primary capillary network). Blood passes from these capillaries into the efferent arterioles, which form a peritubular capillary (secondary) network that will nourish the proximal and distal tubules and carry away absorbed ions and lowmolecular-weight materials. In cortical nephrons the efferent arteriole has a smaller lumen than the afferent arteriole. This inequality serves to promote the filtration pressure in the glomerulus. In juxtamedullary nephrons the efferent arteriole is of the same calibre as the afferent. Veins The interlobular veins receive peritubular capillaries and the stellate veins. These veins end in arcuate veins, which also receive the venule rectae. The arcuate veins join to form interlobar veins, which form the renal vein.

Endocrine system of kidney Juxtaglomerular apparatus The juxtaglomerular apparatus regulates the systemic blood pressure by activation of the renin-angiotensin-aldosterone system. Juxtaglomerular apparatus is the modification of the distal convoluted tubule and the afferent arteriole at the region of their contact (fig. 131).

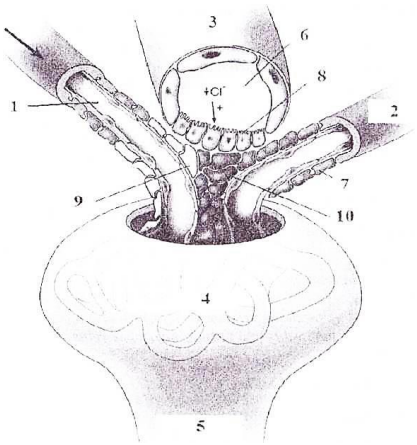


Figure 131. Juxtaglomerular apparatus. 1 - afferent arteriole, 2 - efferent arteriole, 3 - distal convoluted tubule, 4 - glomerulus, 5 - proximal convoluted tubule, 6 - urine, 7 - smooth muscle cells, 8 - macula densa, 9 - juxtaglomerular cells, 10 - extraglomerular mesangial cells

The juxtaglomerular apparatus consists of 3 components:

1**. Macula densa** is an area of closely packed specialised columnar cells in the wall of the distal convoluted tubule. The cells of macula densa aresensitive to the ionic content and water volume of the fluid in the tubule (osmoreceptors). If low

water volume is detected by these cells, they will produce molecular signals that promote renin secretion by other ceils of the juxtaglomerular apparatus, called the juxtaglomerular cells.

2**. Juxtaglomerular cells** are specialised smooth muscle cells in the tunica media of the afferent (and, sometimes, efferent) arteriole. The cytoplasm of these cells contains granules of the enzyme renin. These cells play a critical role in the renin-angiotensin system and thus in renal autoregulation, the self-governance of the kidney.

3. **Extraglomerular mesangial cells** (also known as Goormaghtigh cells) form a conical mass: laterally it is bounded by the afferent and efferent arterioles. These cells are flat and elongated with cytoplasmic processes. Exact function of these cells is not established. It is supposed, that they transfer a signal from the cells of the macula densa to the arterioles and secrete hormone erythropoietin and renin.
4.**Renal interstitium** .Both the cortex and the medulla contain specialized cells in the spaces between the nephrons, collecting tubules, and blood and lymph vessels. These interstitial cells are more frequent in the medulla. Interstitial cells secrete prostaglandin, which participate in regulation of the systemic and renal bloodstream, and vasodilator bradykinin.

Histophysiology of the kidney (urine formation) The kidneys regulate the chemical composition of the internal environment of the organism by a complex process that involves (fig.132):

glomerular filtration;
reabsorption;
secretion.

Filtration takes place in the glomerulus. The glomeruli are composed of blood capillaries in which the hydrostatic pressure - about 45 mm Hg - is higher than in other capillaries. Endothelial cells of glomerular capillaries are fenestrated with numerous openings. The glomerular filtrate has a chemical composition similar to that of blood plasma but contains almost no protein, since macromolecules do not cross the glomerular wall. Selective reabsorption takes place mainly in the proximal convoluted tubules. The substances reabsorbed include water, glucose, aminoacids, proteins of small molecular size, and various ions including sodium, chloride, phosphate, bicarbonate and calcium.

Very large proportion of the water in the glomerular filtrate is reabsorbed through the loops of Henle. Water diffuses passively, following the osmotic gradient. The tlltrate is reduced from an original volume of about 200 litres per day to an average urine output of 1,5 litres per day. **Secretion** is the opposite of reabsorption. This mechanism also changes the composition of urine. Some substances are actively secreted into the tubules. Substances secreted into the urine include ammonia, hydrogen ions, and potassium.

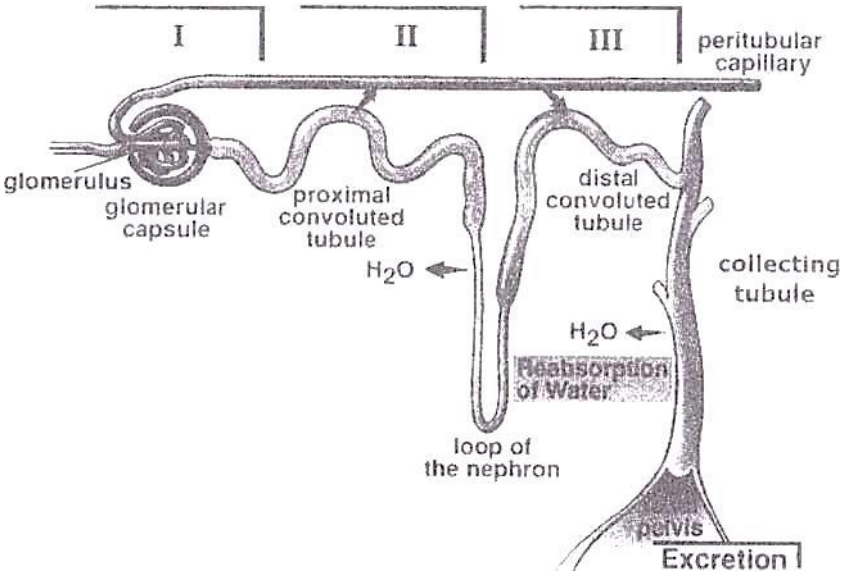


Figure 132. Schematic diagram of urine formation. I - glomerular filtration, IT - selective reabsorption, III - secretion

Urinary passages The calyces, renal pelvis, ureter, and bladder have the same basic histological structure (fig.133).

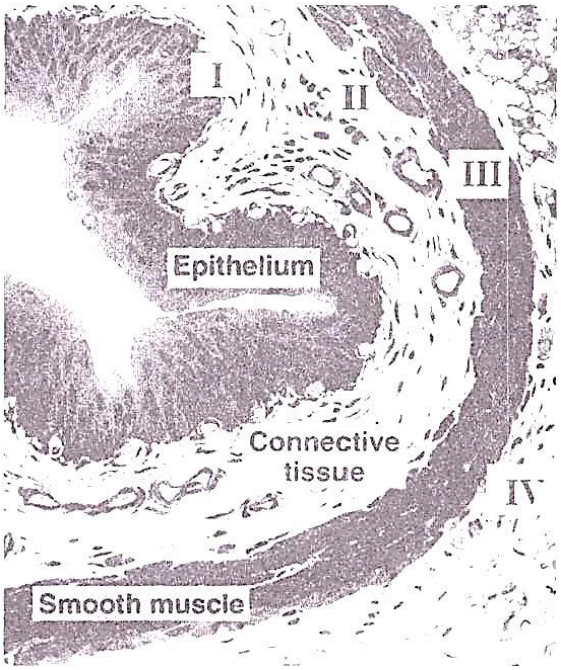


Figure 133. Photomicrograph of cross section of the ureter. I — mucosa, II - submucosa, III — muscularis, IV - outer layer

The wall of these organs consists of 4 layers:

I. Mucosa
II. Submucosa
III. Muscularis
IV. Adventitia

Mucosa consists of:

1) transitional epithelium having 4 or 5 layers of cells;
2) lamina propria which consists of loose connective tissue.

Submucosa consists of loose connective tissue.

Muscularis consists of bundles of smooth muscle cells with intervening connective tissue.

Adventitia consists of loose connective tissue with collagen and elastic fibers. The upper part of the bladder is covered by serous peritoneum. Transitional epithelium having 6 or 8 layers of cells; the superficial cells are rounded and bulge into the lumen in the empty bladder. These cells are frequently polyploid or binucleate. When the epithelium is stretched, as when the bladder is full of urine, the epithelium is only three or four cells in thickness, and the superficial cells become squamous . **Adventitia consists** of loose connective tissue , with blood vessels, lymphatics and nerves.

Urine is squeezed into the bladder by peristalsis

Folds of mucosa help to protect against reflux of urine when the bladder is full.

URETER

Mucosa consists of:

- 1)transitional epithelium having 4 or 5 layers of cells;
- 2) lamina propria which consists of loose connective tissue.

Submucosa consists of loose connective tissue.

Muscularis consists smooth muscle cells with intervening connective tissue.

There is a layer of smooth muscle outside the mucosa:

The upper two-thirds has two layers of smooth muscle: inner longitudinally arranged, and outer circularly arranged.

The lower third has three layers of smooth muscle; Inner longitudinal, middle circular, outer longitudinal.

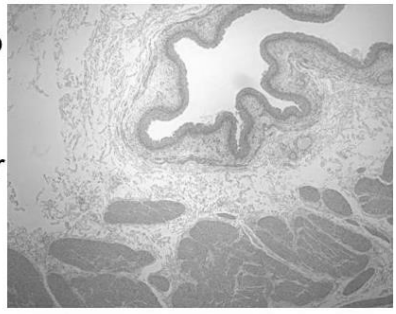
Adventitia consists of loose connective tissue with collagen and elastic fibers.

Urinary bladder

- Its wall has 4 tissue layers;-

1. Tunica mucosa; lined by up to 14 cell layers of transitional epith that rests on lamina propria of loose c. tissue
2. T. submucosa; highly vascular and rich in elastic fibers
3. T. muscularis; has inner and outer longitudinal and middle layer of smooth muscles (dextruser muscles)
4. T. serosa/ adventitia

- The longi muscles form sphincters at ureterovesicular junction to prevent backflow of urine and at neck of bladder to regulate urine emptying



URETHRA

Mucosa consists of:

- 1)The epithelium of the urethra starts off as transitional cells as it exits the bladder. Further along the urethra there are pseudostratified columnar and stratified columnar epithelia, then stratified squamous cells near the external urethral orifice.
- 2) lamina propria which consists of loose connective tissue. There are small mucus-secreting urethral glands, that help protect the epithelium from the corrosive urine

Submucosa consists of loose connective tissue.

Muscularis consists smooth muscle cells, has two layers of smooth muscle: Inner longitudinal, outer circular.

Adventitia consists of loose connective tissue.

Histology of the Female Urethra

The urethra in females is short. It is only about about 1.5 inches lengthwise. The lining epithelium of the female urethra is psuedostratified columnar epithelium and stratified sqauamous epithelium.

Histology of Male Urethra

The urethra in the male is longer than the urethra of females. The male urethra is 7 to 8 inches lengthwise. The male urethra fuctions as a conduit for urine and semen. The male urethra is divided into three sections: prostatic urethra, membranous urethra, and spongy (penile) urethra.

Histology of the Prostatic Urethra

The first portion of the male urethra is the prostatic urethra. This portion of the urethra goes through the prostate gland. The prostatic urethra is lined by transitional epithelium.

Histology of the Membranous Urethra

he second part of the male urethra is the membranous urethra. This is a short segment. The lining epithelium of the membranous urethra is psuedostratified columnar epithelium.

Histology of the Spongy Urethra

The third part of the urethra is the spongy urethra. The spongy urethra is also called the penile urethra. This is the longest section of the male urethra. It travels through the corpus spongiosum of the penis. The lining epithelium of the spongy urethra is psuedostratified columnar epithelium which then transitions to stratified squamous.

Development of the kidney The human kidney has passed through three stages of evolution:

pronephros,
mesonephros,
metanephros.

Pronephros is formed from the nephrogenic cord of the cervical region (fig.134 - 1). The human pronephros has not connection with blood system, is non-

functional, and disappears soon after its formation. Nephric duct formed in relation to the pronephros and ending in the cloaca, however, persists.

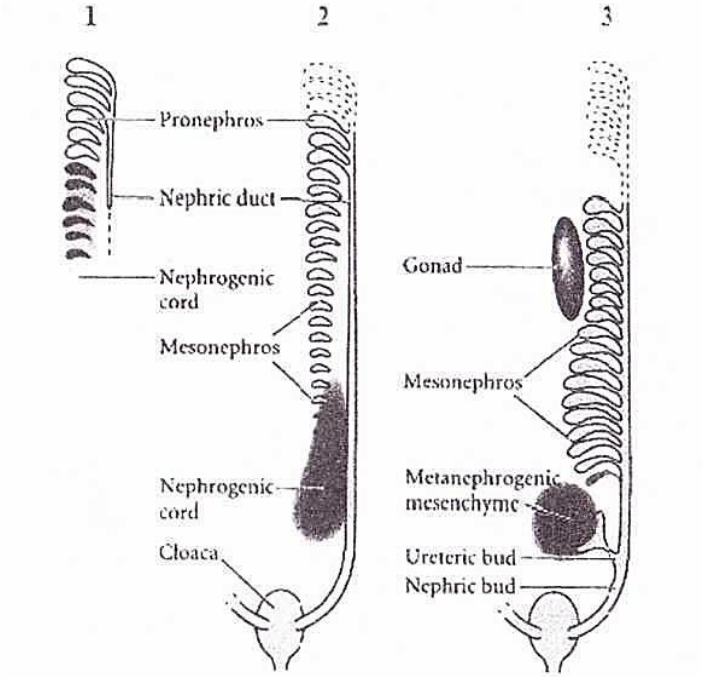


Figure 134. General scheme of development of the kidney.

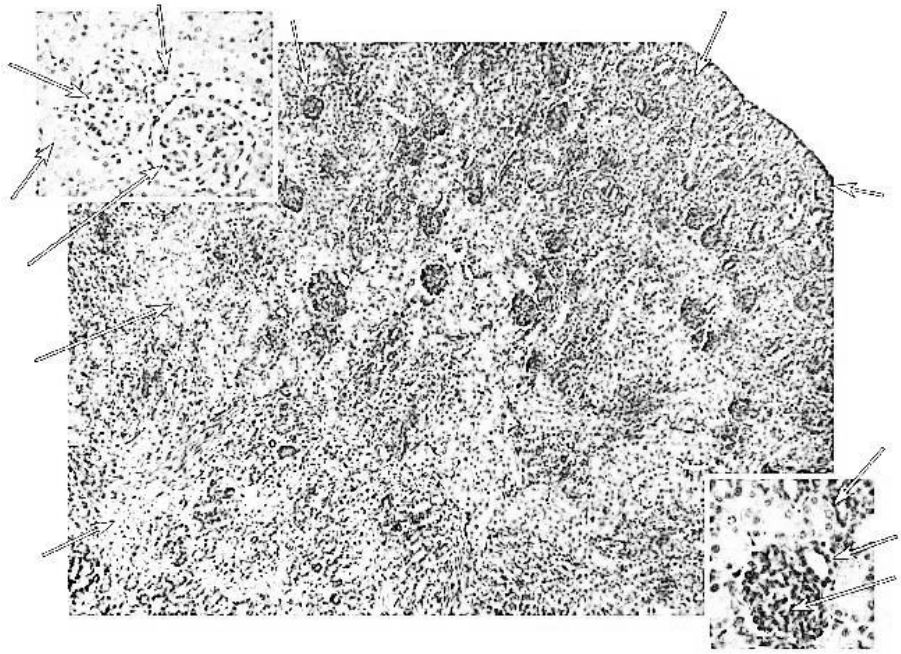
Mesonephros (flg.134-2) consists of a series of excretory tubules that develop in the thoracolumbar region. These tubules drain into the nephric duct which may now be called the mesonephric duct. Most of the mesonephric tubules disappear, but some of them are modified and take part in forming the duct system of the testis.

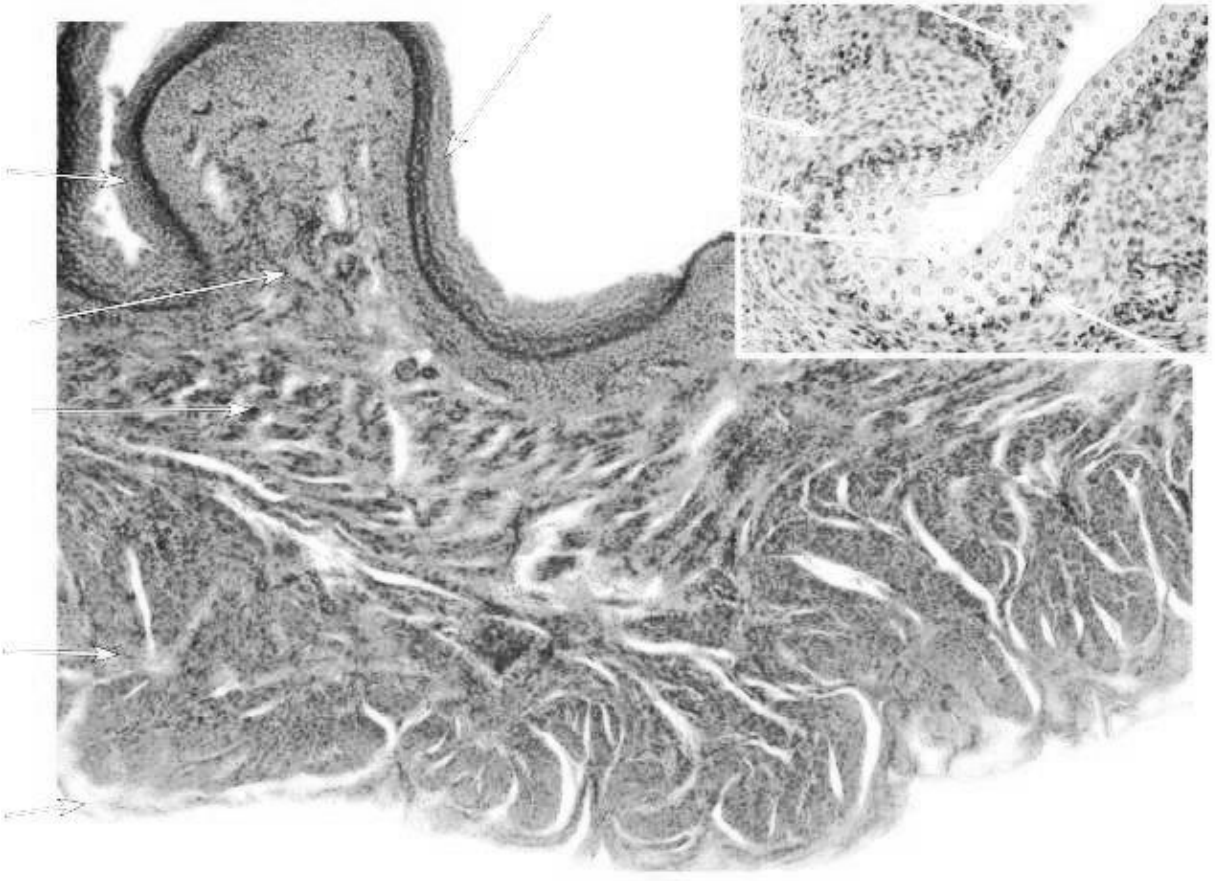
Definitive kidney (fig.134 -3) arises from two distinct sources. The ureters, the pelvis, calyces, papillary ducts and collecting tubules of the kidney are derived from the mesonephric duct. The nephrons are derived from the lowest part of the nephrogenic cord the cells of which form the metanephric blastema. The ends of the nephrons dilate and become invaginated by a mass of mesodermal tissue. This tissue differentiates to form the glomerulus.

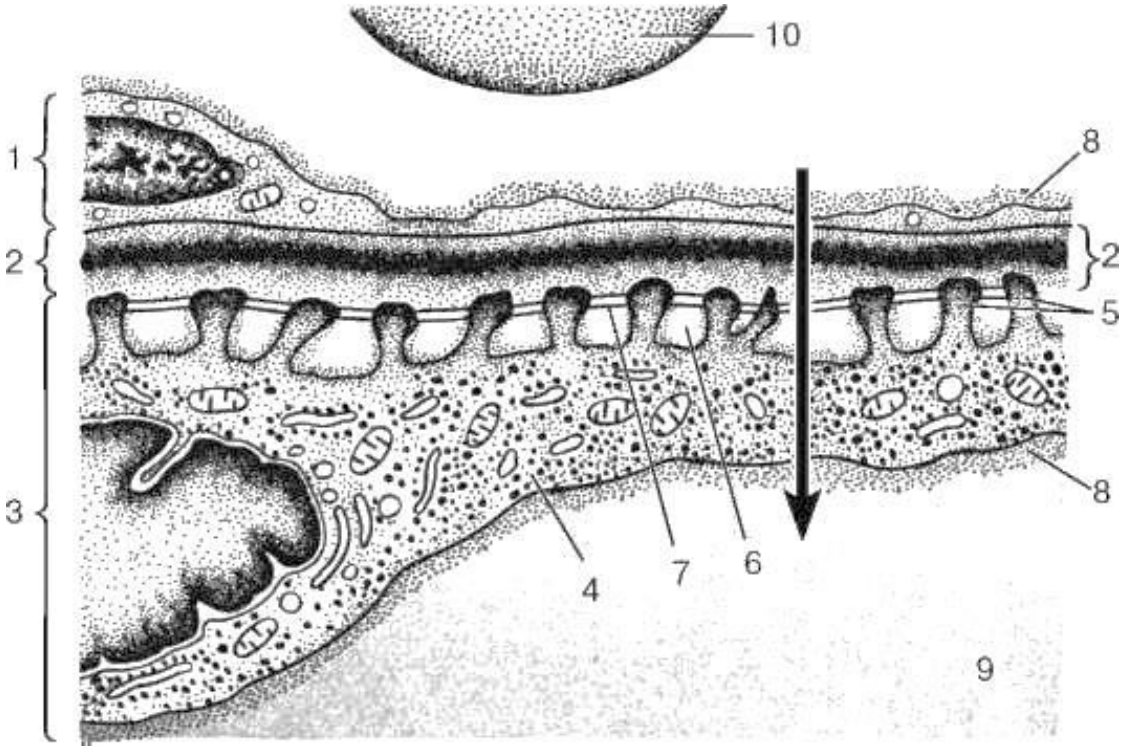
Practical lessons

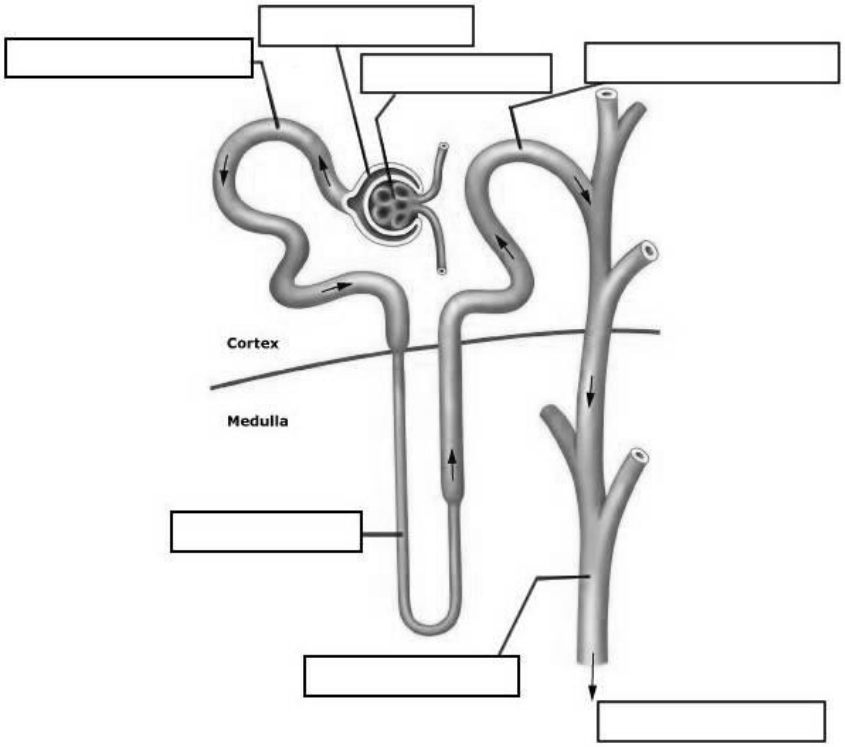
1. Kidneys. Structure and functions of the cortical nephron.
2. Kidneys: endocrine apparatus, function.
3. Development of the kidney.
4. Urinary passages.

Paint and mark basic histological structure









Signature of teacher_____

MALE REPRODUCTIVE SYSTEM . Overview of the male reproductive system The human male reproductive system consists of a number of sex organs that are a part of the human reproductive process.

The male reproductive system is composed of:

- testes,
- genital excurrent ducts,
- accessory glands (prostate gland, seminal vesicles, bulbo-urethral glands),
- copulatory organ (penis).

Functions of the male reproductive system:

- reproductive (production of the male gametes- spermatozoa),
- endocrine (production of the androgen (male sex hormone) - testosterone).

Testis .The testis is surrounded by a thick connective tissue capsule called tunica albuginea. On the posterior surface of the testis the tunica albuginea forms the mediastinum (fig.135).

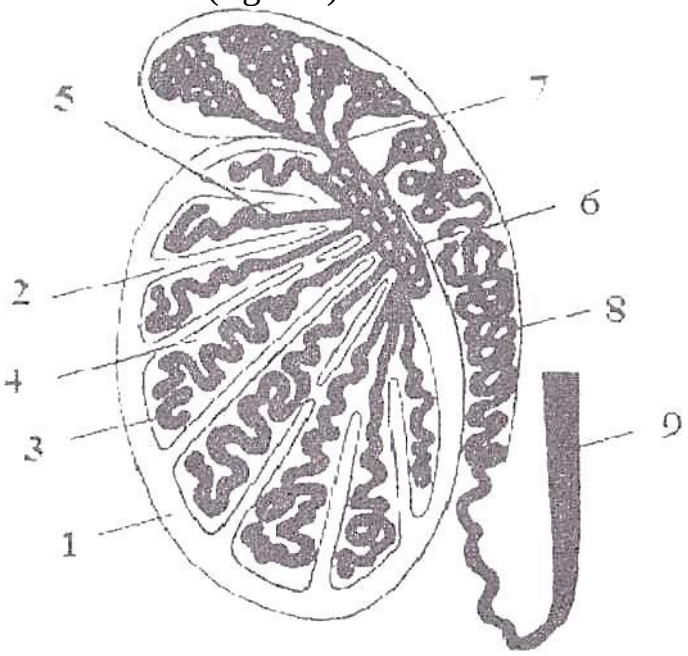


Figure 135. Schematic diagram of a testis. 1 - tunica albuginea, 2 - septum. 3 - seminiferous tubules. 4 - interstitium, 5 - straight tubules, 6 - rete testis, 7 - efferent ductules, 8 - duct of epididymis, 9 - ductus deferens

Connective tissue septa penetrate the giand and divide it into 250 pyramidal lobules. Each lobule is occupied by 1- 4 convoluted seminiferous tubules, which form a network. These are sperm producing tubules.

Convoluted seminiferous tubules .The convoluted seminiferous tubules (fig.136) consist of:

- **fibrous tunica propria and**
- complex stratified seminiferous, germinal, or spermatogenic, epithelium. **Tunica propria consists of several layers**.

  1) **. Basal layer** consists of thin collagen fibers and is located between the basal membranes of germinal epithelium and myoid cells.

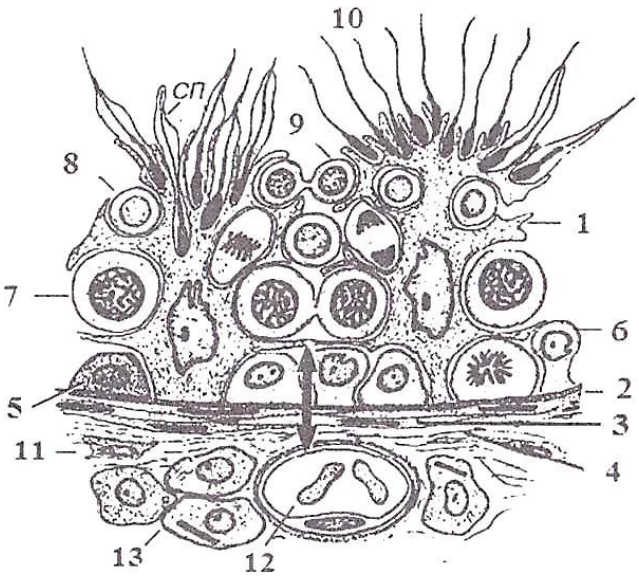


Figure 136. Seminiferous tubule wall. 1 - Sertoli cell, 2 - basal layer, 3 - mvoid cells. 4 - external fibrous layer, 5 - type A spermatogonium, 6 - type B spermatogonium, 7 - primary spermatocyte, 8 - secondary spermatocyte, 9 - spermatids, 1 0 - spermatozoa, 1 1 - interstitium, 1 2 - blood capillary, 13 - Leydig cells, 14 - tight junctions between Sertoli cells, arrow shows blood testis barrier

2). Myoid layer consists of spindle-shaped myofibroblastes (myoid ceiis) which exhibit smooth muscle characteristic; the contractile activity of these cells aids movement of spermatozoa along the tubules.

3 **). External Jibrous layer** consists of collagen fiber and fibroblasts

Seminiferous epithelium. Seminiferous epithelium consists of 2 basic cell populations:

1) **spermatogenic cells** in different stages of their development and

2**) Sertoli** (supporting) cells.

Spermatogenic cells. Spermatogenie cells (fig.137) are arranged in concentric layers (5 or 6) and differentiate progressively from the periphery to the lumen of the tubule:

- **spermatogonia** (types A and B) are the undifferentiated germ cells, are located at the periphery of the tubule; spermatogonia type A are stem cells for spermatogenic lineage that are classed as type A dark (Ad) or A pale (Ap); type Ad are true stem cells; spermatogonia type B are progenitor ceil for primary spermatocyte;
- **primary spermatocytes** (46 chromosomes, 4N DNA) are found in the middle of the seminiferous tubule; primary spermatocyte results from the growth and differentiation of one type B spermatogonium;
- **secondary spermatocytes** (23 chromosomes, 2N DNA) arise from the division of primary spermatocytes; they are located near the lumen of the seminiferous tubule;
- **spermatids** (23 chromosomes, IN DNA) are small cells with coSertoli (supporting) cells Sertoli (supporting) cells (fig.137) are tall pyramidal cells. The bases of the Sertoli cells rest on the basal lamina, apical ends extend into the lumen of the seminiferous tubule.

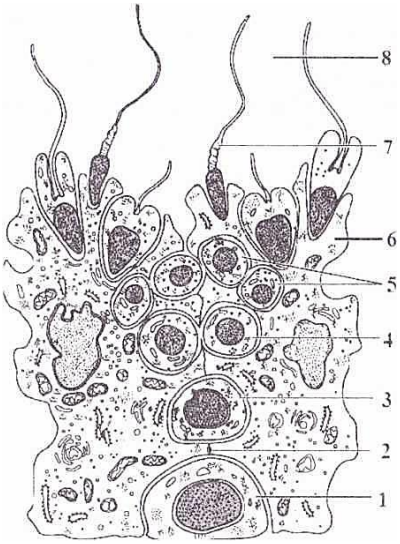


Figure 137. Seminiferous epithelium. 1 - spermatogonium, 2 - tight junction, 3 — primary spermatocyte, 4 — secondary spermatocyte, 5 - spermatid, 6 - Sertoli cell, 7 — spermatozoon, 8 — lumen of seminiferous tubule

Functions of Sertoli celts:

1) support, protection, and nutrition of the developing spermatozoa;
2) phagocytosis of cytoplasmic fragments, which form during spermatogenes is;
3) secretion of:

- into the seminiferous tubules a fluid that Hows in the direction of the genital ducts and is used for sperm transport;
- androgen binding protein that serves to concentrate testosterone in the seminiferous tubule; it is necessary for spermatogenesis;
- sexual steroids - estrogens and testosterone;
- peptides inhibin and activin, which suppress and activate FSH synthesis and release in the anterior pituitary gland,
- antimullerian hormone that promotes the normal development of the male reproductive system.

Sertoli cells are bound together by tight junctions between their lateral processes at the level of spermatogonia. Lateral processes of Sertoli cells divide the seminiferous epithelium into **2 compartments**:

- **basal (abluminal**) compartment and
- **adluminal compartment**.

The basal compartment contains spermatogonia and has free access to materials found in the blood. The adluminal compartment contains spermatocytes, spermatids and spermatozoa. B Blood-testis barrier **The blood-testis barrier** (fig.136) is a barrier between the blood vessels and the seminiferous tubules. The barrier prevents passage of cytotoxic agents (substances that are toxic to cells) into the seminiferous tubules. **This barrier protects also the developing sperm cells from immunologic attack and consists of:**

- **endothelial cells of blood capillary of interstitial connective tissue;**
- **basal lamina of endothelial cells;**

- **interstitial connective tissue;**
- **tunica propria of seminiferous tubule;**
- **tight junctions between lateral processes of Sertoli cells**.

Endocrine function of the testis.The spaces between the seminiferous tubules are filled with interstitial connective tissue, nerves, blood and lymphatic vessels. The principal cells of interstitial tissue are the **interstitial, or Leydig**, cells, which have the characteristic of steroid-secreting ceils (fig.136).

Leydig cells are rounded in shape, have a central located nuclei and an eosinophilic cytoplasm. These cells produce the male steroid hormone testosterone, which is responsible for the development of male reproductive tissues such as the testis and prostate as well as promoting secondary sexual characteristics such as increased muscle and bone mass and hair growth. 0 Spermatogenesis Spermatogenesis is the process of differentiation of the male germ cells. The mature male functional sperm cells are produced within the seminiferous tubules of the testes.

Spermatogenesis can be divided into 3 phases (fig.138):

I. **Spermatogonial phase (**mitosis) begins with the spermatogonia, situated in the basal compartment of seminiferous epithelium. These cells undergo serious mitoses, and newly formed cells can follow' one or two paths: they can continue, after one or more mitotic divisions, as stem cells, or type A spermatogonia or they can differentiate during progressive mitotic cycles to become type B spermatogonia. Type A spermatogonia are the stem cells, type B spermatogonia are the progenitor cells that differentiate into primary spermatocytes (46 chromosomes, 4N DNA).

II. **Spermatocyte phase** (meiosis), during which primary spermatocytes undergo two successive divisions, to reduce both half of chromosome number and the amount of DNA, producing spermatids. Meiotic division (I) of a primary spermatocyte gives rise to a pair of secondary spermatocytes (23 chromosomes, 2N DNA); meiotic division (II) of a secondary spermatocyte gives rise to a pair of spermatids (23 chromosomes, IN DNA). Because there is no S phase (DNA synthesis) between the first and second meiotic divisions of the spermatocytes, the amount of DNA per cell is reduced by half in this second division, forming haploid (IN) cells. This process occurs in the adluminal compartment of seminiferous epithelium.

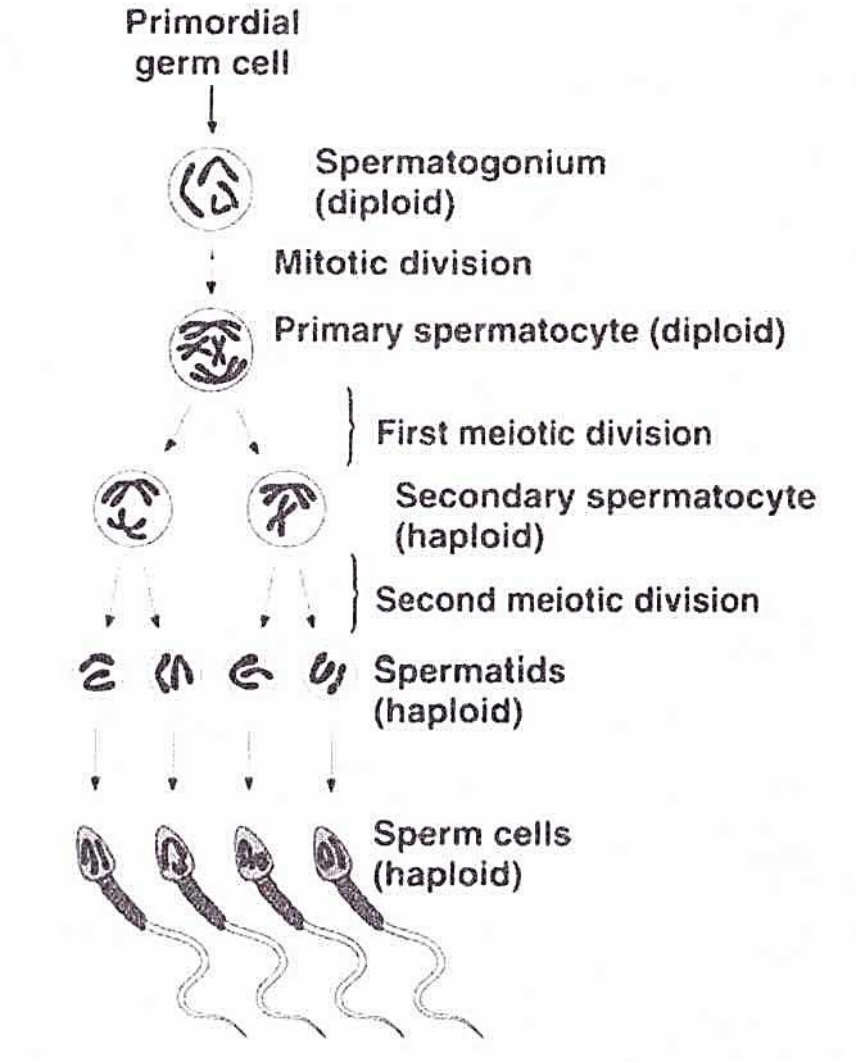


Figure 138. Schematic diagram illustrating spermatogenesis.

II. **Spermatid phase** (spermiogenesis), during which the spermatids go through process of cytodifferentiation, producing spermatozoa. Spermatids undergo spermiogenesis, a complex of differentiation that includes (fig.139)

- formation of the acrosome,
- condensation and elongation of the nucleus,
- formation of the flagellum,
- loss of much of the cytoplasm.

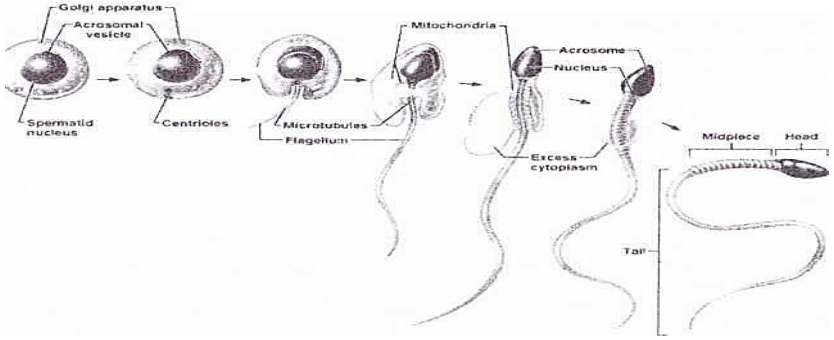


Figure 139. Schematic diagram illustrating spermiogenesis.

The end result is the mature spermatozoa, which are then released into the lumen of the seminiferous tubule. Complete cycle (gonia to zoa) takes 60 to 70 days.

Influencing factors. The process of spermatogenesis is highly sensitive to fluctuations in the environment, particularly hormones and temperature. Testosterone is required in large local concentrations to maintain the process, which is achieved via the binding of testosterone by androgen binding protein present in the seminiferous tubules. Testosterone is produced by interstitial cells (Leydig cells). Seminiferous epithelium is sensitive to elevated temperature, and will be adversely affected by temperatures as high as normal body temperature. Consequently, the testes are located outside the body in a sack of skin called the scrotum. Dietary deficiencies (such as vitamins B, E and A), anabolic steroids, metals (cadmium and lead). X-ray exposure, dioxin. alcohol, and infectious diseases will also adversely affect the rate of spermatogenesis.

Male genital ducts. The male genital ducts are subdivided into:

- **intratesticular and**
- **excurrent** ducts.

Intratesticular ducts. Intratesticular ducts are the **tubuli recti, the rete testis, and the efferent ductules.** At the termination of each convoluted seminiferous tubule, the lumen narrows and continues in short segments, called tubuli recti (straight tubules). **Tubuli recti** connect the convoluted tubules to a labyrinth of the mediastinum, the rete testis. The **rete is connected** to theportion of the **epididymis by ductuli efferentes**. The ductuli efferentes fuse to form the ductus epididymis. Tubuli recti are lined with Sertoli cells in an initial part, in the distal part - simple cuboidal epithelium. Rete testis is a highly anastomotic network of channels lined with simple cuboidal epithelium. From the rete testis 10-20 efferent ductules extend that form the head of the epididymis. Efferent ductules consist of (fig.140, 141):

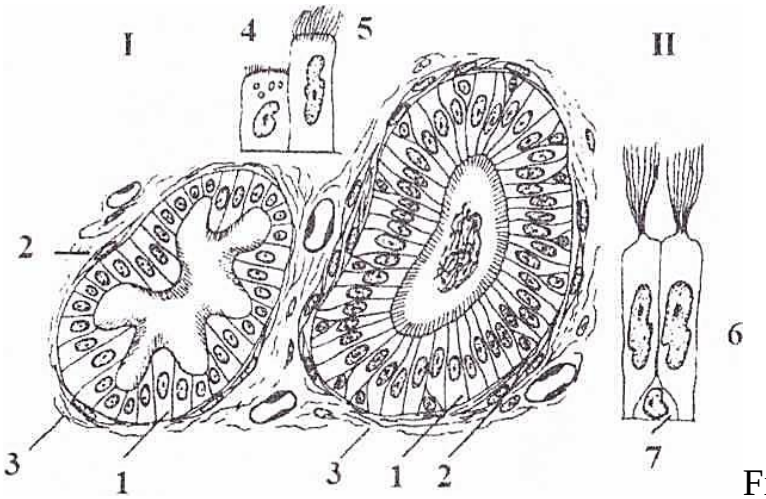


Figure 140. Schematic diagram of efferent ductule of epididymis (I) and duct of epididymis (II). 1 - mucosa, 2 - muscularis, 3 - adventitia, 4 - nonciliated cuboidal cell, 5 - columnar ciliated cell, 6 — principal cell, 7 - basal cell.

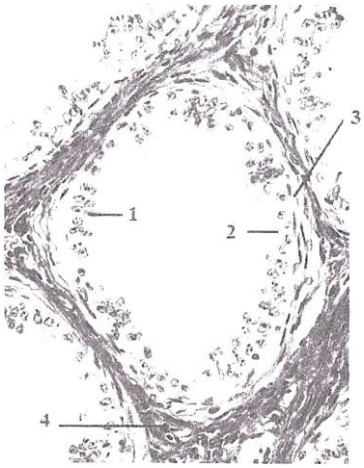


Figure 141. Photomicrograph of efferent ductule of epididymis. 1 - pseudostratified columnar epithelium, 2 — lamina propria

I. **mucosa** which contains:
1) pseudostratified columnar epithelium composed of:
- columnar ciliated cells that promote the transport of spermatozoa toward the ductus epididymis;
- nonciliated cuboidal cells that absorb much of the fluid secreted by the seminiferous tubules;
2) lamina propria is composed of loose connective tissue;

II. **muscularis** is composed of circularly oriented smooth muscle cells;

III. **adventitia** consists of loose connective tissue.

Excurrent ducts Excurrent ducts are the duct of epididymis, which forms the epididymis, the ductus (vas) deferens and the ejaculatory duct. Duct of **epididymis consists** of (fig.140,142):

I. **Mucosa** which contains:

1) pseudostratified columnar epithelium that composed of:
- tall columnar (principal) cells with long microvilli (stereocilia);
- basal cells that are the stem cells;

2) lamina propria is composed of loose connective tissue;

II. **Muscularis** is composed of smooth muscle cells whose peristaltic contractions help to move the sperm along the duct;

III. **Adventitia** consists of loose connective tissue.

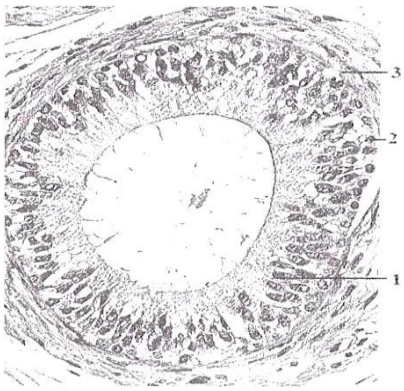


Figure 142. Photomicrograph of duct of epididymis. 1 - principal columnar cells, 2 - basal cells, 3 - smooth muscle cells

Ductus (vas) deferens is the continuation of the ductus epididymis; it empties into the prostatic urethra. The ductus deferens has a thick wall but a small lumen. The **wall of the ductus deferens consists of 3 layers** (fig.143):

I. **Mucosa** forms longitudinal folds and comprises:

1) pseudostratified columnar epithelium that composed of:

- columnar cells with stereocilia;
- basal cells that are the stem cells;

2)lamina propria is composed of loose connective tissue rich in elastic fibers;

II. **Muscularis** consists of longitudinal inner and outer layers separated by a circular layer;

III. **Adventitia** consists of loose connective tissue.

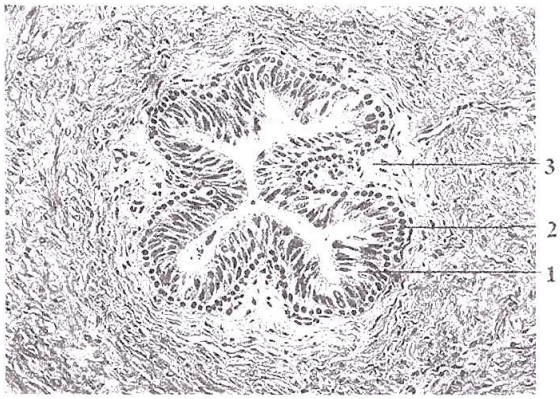


Figure 143. Photomicrograph of ductus deferens. 1 - pseudostratified columnar epithelium. 2 — basal cells, 3 — lamina propria

Ejaculatory duct connects the ductus deferens to prostatic urethra.

I. **Mucosa** has many folds and is lined by

1) pseudostratified columnar epithelium, containing tall secretory cells;

2) lamina propria is composed of loose connective tissue with elastic fibers.

II. **Muscularis is absent**; the fibromuscular tissue of the prostate substitutes it. The ejaculatory duct is supported by fibrous tissue of the prostate.

Accessory genital glands The accessory genital glands are :

- prostate gland,
- seminal vesicles,
- bulbourethral glands.

Prostate gland. The prostate gland is the largest accessory sex gland which surrounds the bladder neck and the first part of the urethra. The prostate gland is covered by connective tissue capsule rich in smooth muscle cells. From capsule incomplete septa extend and divide the gland into 50 or so lobules. The fibromuscular stroma surrounds the glands. The gland is composed of about 30 to 50 compound tubulo- alveolar prostatic glands which are divided on 3 groups (fig.144):

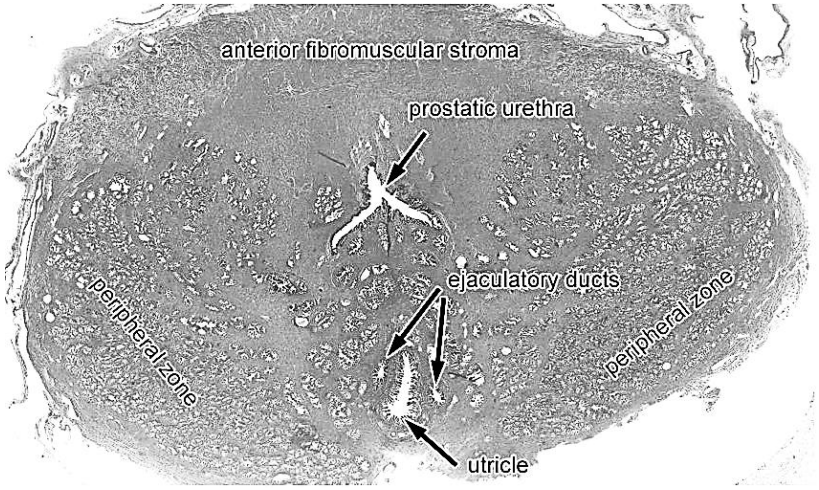


Figure 144. Diagram of prostatic glands. 1 - urethra, 2 - mucosal (central zone), 3 - submucosal (transitional zone), 4 - main (peripheral zone)

- **mucosal (central zone**),
- **submucosal (transitional zone)**,
- **main (peripheral zone**).

The prostatic glands (llg.145) consist of:

1. **secretory portions,**
2. **duct system**.

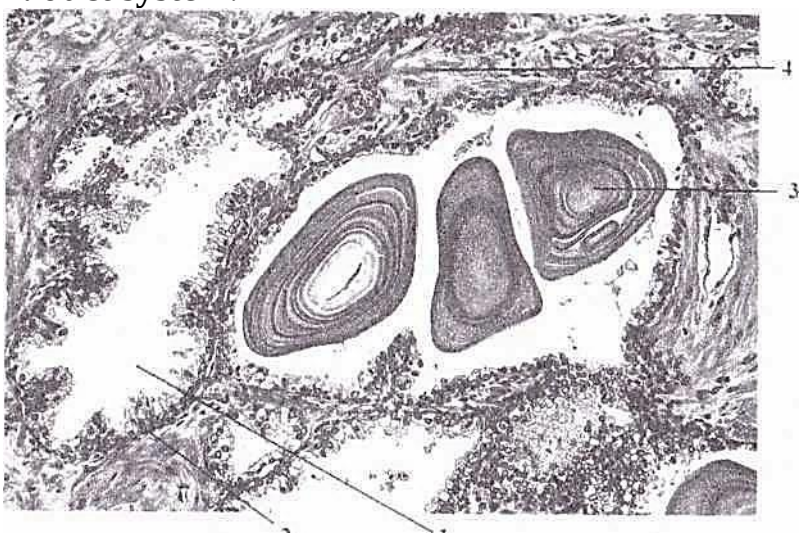


Figure 145. Photomicrograph of a prostate gland. 1 - mucosal glands, 2 - prostatic epithelium. 3 - prostatic concretions, 4 - fibromuscular stroma

The secretory portions of prostatic gland are lined by a pseudostratified columnar epithelium which consists of **3 types of cells**:

- **columnar** with basally located nuclei;
- **basal** which are located along the basement membrane;
- **endocrine** which secrete serotonin, somatostatin, and other peptides influencing on secretory activity of epithelium and contractility of smooth muscle cells of stroma. Small spherical bodies of glycoproteins composition are frequently observed in the lumen of prostatic glands. These bodies are often calcified. They are called prostatic concretions. Their significance is not understood. Their number increases with age. The secretion of the prostate is fluid with a slight acidic reaction and is rich in an enzyme called

acid phosphatase. The secretion nourishes the spermatozoa. The ducts of the glands of mucosal layer secrete directly into urethra; the other two layers have ducts that open into the prostatic sinuses located on the utethral crest.

Seminal vesicles. The seminal vesicles (fig.146)

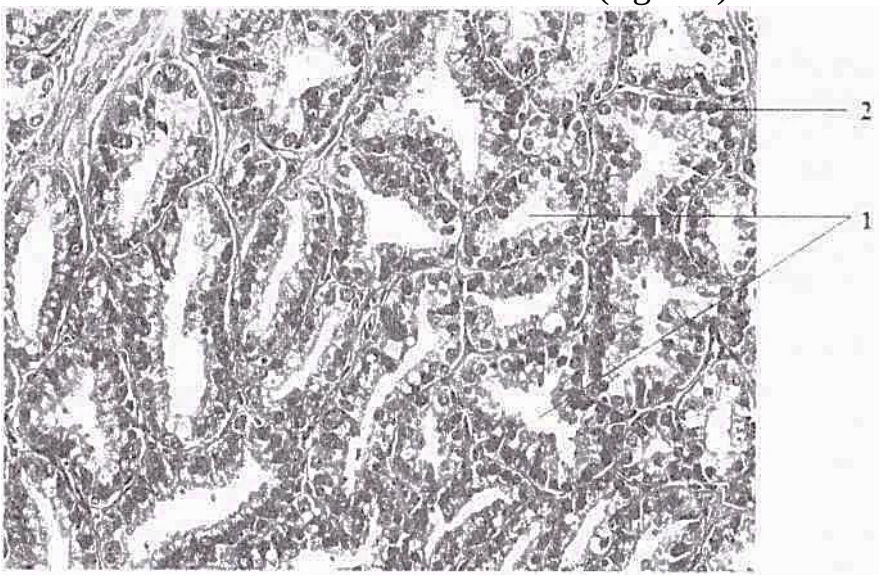


Figure 146. Photomicrograph of human seminal vesicle. 1 - lumens of glands, 2 - pseudostratified columnar epithelium of the glandsare paired sacculated **glands consisting of**:

I. **mucosa** which has many branched folds and comprises:

1) pseudostratified columnar epithelium;

2) lamina propria which is composed of loose connective tissue with elastic fibers;

II. muscularis which consists of outer longitudinal and inner circular layer of smooth muscle tissue.

III. adventitia merges with the surrounding connective tissue. The viscid secretion of the seminal vesicles contains spermatozoaactivating substances such as fructose, citrate, prostaglandins, and several proteins.

Bulbourethral glands (Cowper's glands). The bulbourethral glands are located proximal to the membranous portion of the urethra and empty into it. They are compound tubulo-alveolar glands lined with mucus-secreting simple euboidal epithelium. Skeletal and smooth muscle cells are present in the septa that divide each gland into lobes. The secretion is clear mucus, contains galactose, galactosamine, galacturonic acid, sialic acid and acts as a lubricant.

Penis. The penis is the male copulatory organ. When the male becomes sexually aroused, the penis becomes erect and ready for sexual activity. The erectile tissue of the penis contains a specialized arrangement of arteries, shunts, and venous sinusoids within a matrix of connective tissue and smooth muscle. The erectile tissue is organized into paired dorsal corpora cavernosa and one ventral corpus spongiosum. The corpora cavernosa are surrounded by tough fibrous connective tissue, the tunica albuginea. Between this sheath and the overlying skin is a layer of very loose elastic connective tissue (Buck's fascia) that permits the skin of the penis to move freely along the shaft. The skin includes a smooth muscle layer (the

dartos). The penile urethra passes through the corpus spongiosum, where it is associated with small mucous glands of Littre.

Development of the reproductive systems. The genetic sex of a child is determined at fertilization by presence or absence of the Y chromosome. The reproductive organs are developed from the intermediate mesoderm. The permanent organs of the adult are preceded by the structures which disappear before the end of fetal life. These embryonic structures are two primitive ducts that adjacent to each developing gonad and can give rise to either the male or the female reproductive tracts. The Wolffian (mesonephric) ducts are more medial. The Mullerian (paramesonephric) ducts are more lateral, but then fuse in the midline more caudally (fig.147).

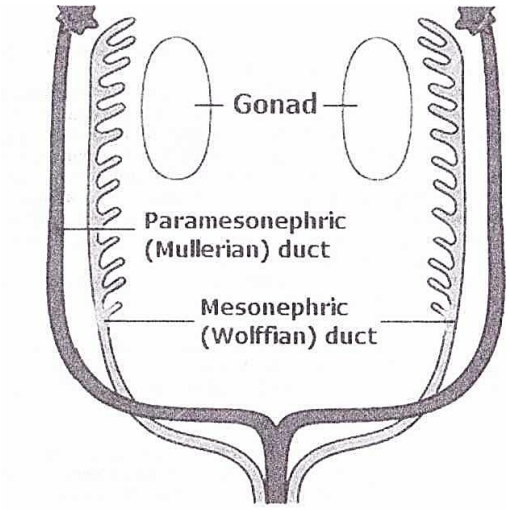


Figure 147. Schematic diagram of the indifferent stage.

The Wolffian duct remains as the duct in males, and the Mullerian as that of the female. During embryonic development there is a sexually indifferent stage in which the embryo has the potential to develop either male or female structures. Sexual differentiation begins with sexual determination, which depends upon the sex chromosomes, X and Y. Sexual determination involves the specification of the gonads as either testes or ovaries. If the embryo is XY, the presence of the SRY gene (sex-determining region of the Y chromosome) will direct the gonads to develop as testes. In the absence of a Y chromosome and SRY gene, the gonads develop as ovaries. Once the gonad begins to develop as a testis, the two types of cells in the testis differentiate and begin to generate important regulatory molecules that direct sexual differentiation. The Leydig cells producetes testerone, which promotes development of the Wolffian ducts. The Wolffian ducts then differentiate to form the epididymis, vas deferens, seminal vesicles, and ejaculatory' ducts. The Sertoli cells produce Mullerian inhibiting substance (MIS), a peptide hormone which causes the Mullerian ducts to regress. Female development proceeds when there is an absence of the SRY gene. No testosterone or MIS is made. The Wolffian ducts regress, and the Mullerian ducts persist, developing into the

fallopian tubes, the uterus and the upper part of the vagina. The gonads develop in close association with the urinary system. The testes (like ovaries) are derived from **three sources:**

intermediate mesoderm forms longitudinal elevation along dorsal body wall - urogenital ridge;

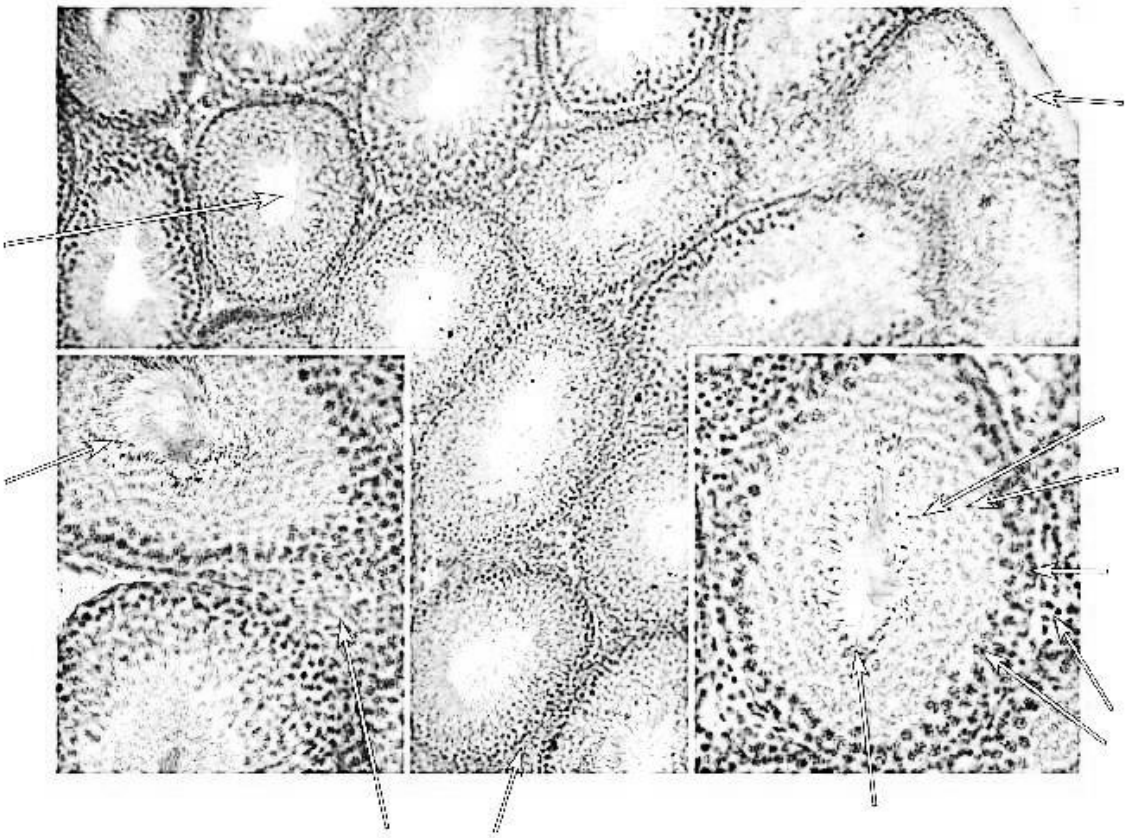
mesodermal epithelium that lines the urogenital ridges form gonadal ridge,

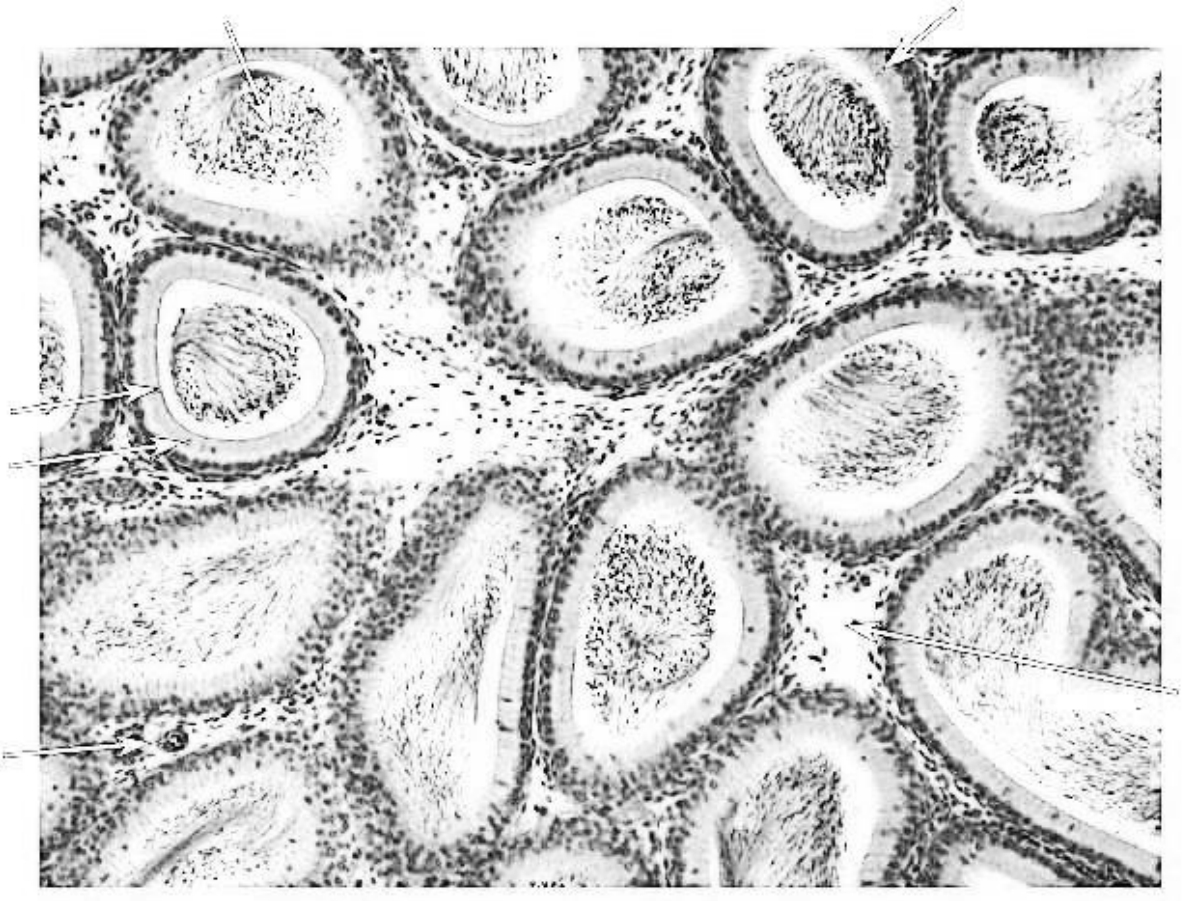
formation of primary sex cords from gonadal ridge, migration of primordial germ cell from the yolk sac; later sex cords differentiate into gonads.

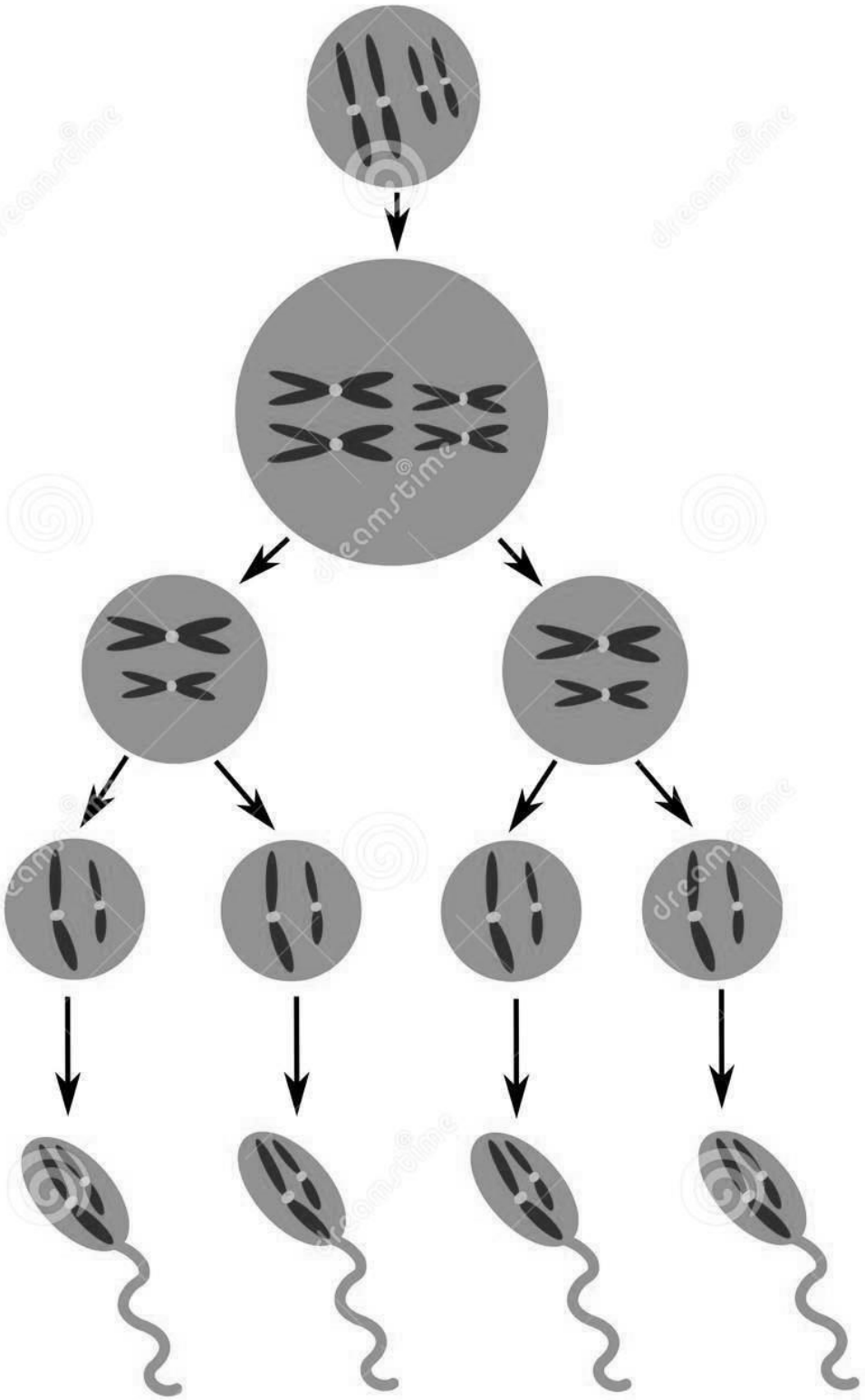
Practical lessons

1. Testis: structure and functions.
2. Spermatogenic cells.
3. Epididymis and prostate gland: structure and functions.
4. Development of the reproductive systems.

Paint and mark basic histological structure







Signature of teacher_____

FEMALE REPRODUCTIVE SYSTEM

Overview of the female reproductive system **The female reproductive system is composed of:**

- **internal organs** (ovaries, uterine tubes, uterus, and vagina) (fig.148),
- **external genitalia** (mons pubis, labia majora and minora, clitoris, vestibule and opening of the vagina, and external urethral orifis)

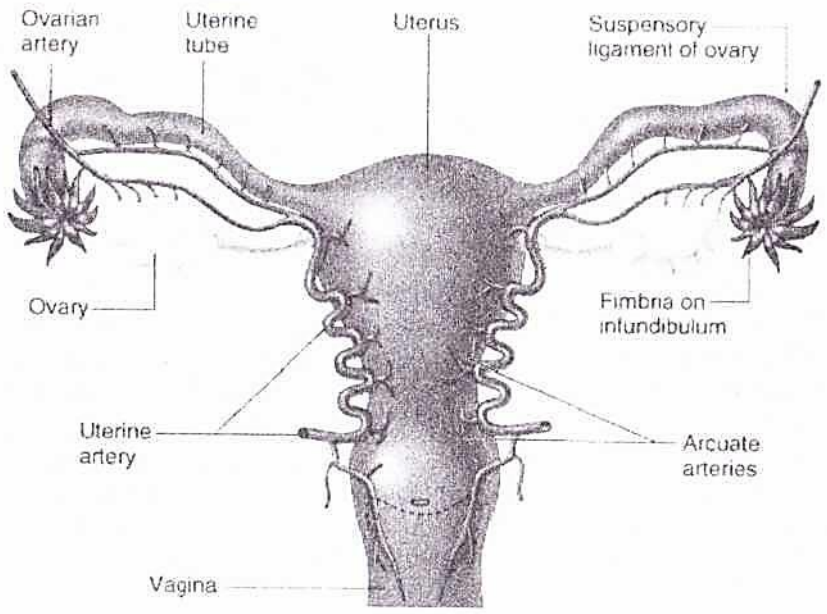


Figure 148. Schematic diagram of female sex organs.

Functions of the female reproductive system

- **reproductive** (production of gametes - ova); >
- **endocrine** (production and secretion of female sex hormones: estrogens and progesterone).

Ovary 1 he surface of the ovary is covered by a single layer of cuboidal epithelium (**germinal epithelium).** Connective tissue forms a thin **capsule** called tunica albuginea. Ovary is divided into an outer **cortex and an inner medulla** (fig.149). The medulla is composed of loose connective tissue, which contains blood vessels and nerves. The cortex consists of connective tissue stroma in which the ovarian follicles are embedded.

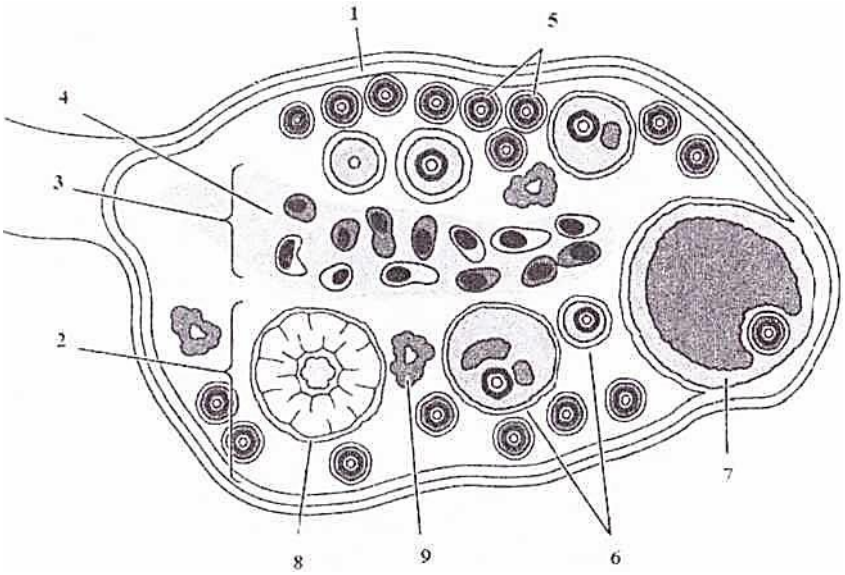


Figure 149. Schematic diagram of the ovary. 1 - tunica albuginea, 2 - cortex, 3 - medulla, 4 - blood vessels, 5 - primordial follicles, 6 - growing follicles, 7 — preovulatory follicle. 8 — corpus luteum, 9 - corpus albicans

Ovarian follicles. The ovarian follicles consist of one oocyte surrounding by follicular cells. **Types of ovarian follicles**:

- **primordial follicles;**
- **growing follicles: primary and secondary;**
- **mature (tertiary, preovulatory, Graafian) follicles.**

The primordial follicles (fig.150) are found in the peripheral part of cortex. **Primordial follicle** consists of the oocyte in prophase of the first meiotic division surrounding by a single layer of squamous follicle cells. The outer surface of the follicle cells is bounded by a basal lamina.

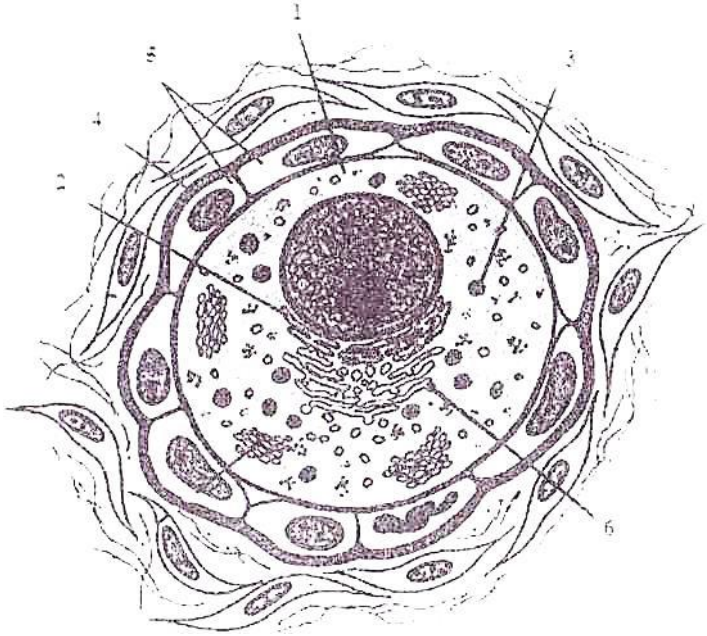


Figure 150. Primordial follicle. 1 - oocyte, 2 - rER, 3 - mitochondrion, 4 - basal lamina, 5 - follicle cells, 6 - Golgi complex (from Ross M.H., 2003)

The primary follicle consists of the oocyte surrounding by a single layer of cuboidal or columnar follicular (granulosa) cells (fig.151). A homogeneous, deeply staining, acidophilic refractive layer called zona pellucida (glycoproteins between the oocyte and granulosa cells) becomes visible. Zona pellucida is secreted by growing oocyte and follicular cells.

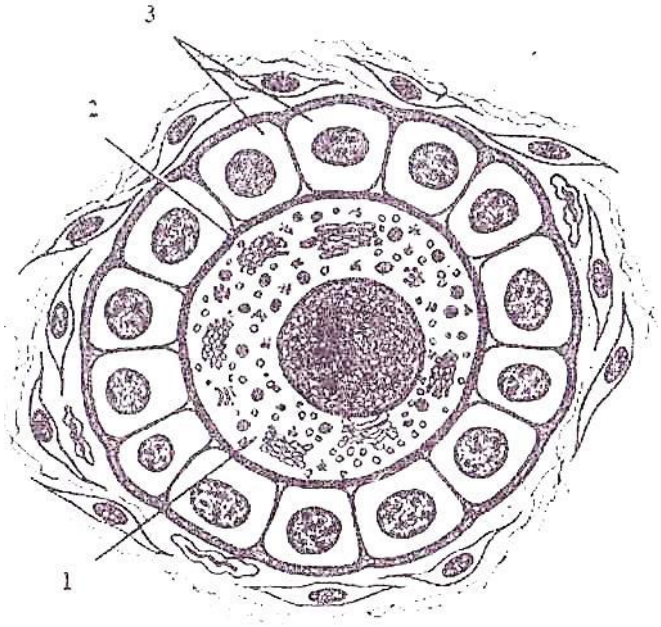


Figure 151. Primary follicle. 1 — oocyte, 2 - forming zona pellucida, 3 - follicle cells (from Ross M.H., 2003)

Late primary follicles. The continued proliferation of granulosa cells will result in the formation of the stratified epithelium surrounding the oocyte (fig.152). Connective tissue cells surrounding the follicle form concentric sheaths, the thecafolliculi.

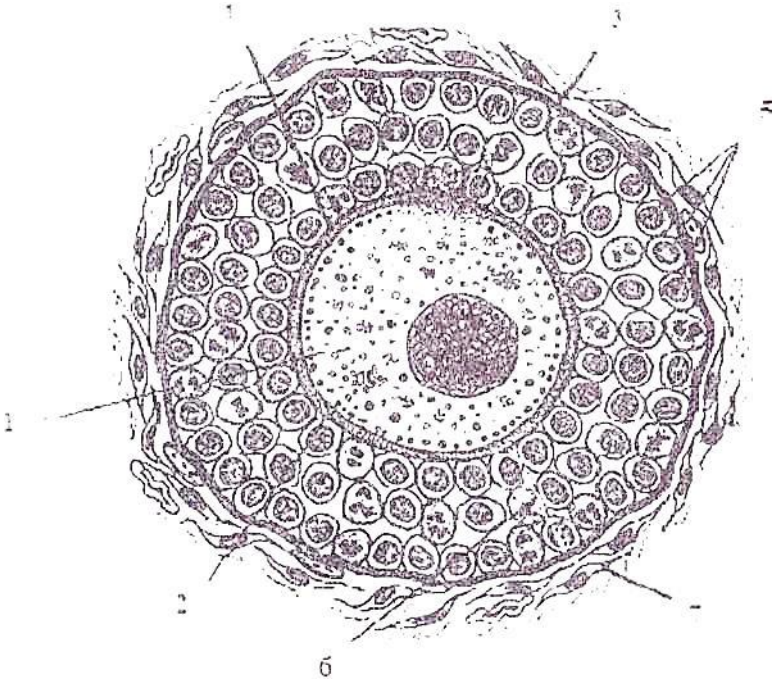


Figure 152. Late primary follicle. 1 - oocyte, 2 - cortical granules, 3 - basal lamina, 4 - zona pellucida, 5 - granulosa cells, 6 - stratum granulosum, 7 - theca folliculi (from Ross M.H., 2003)

Secondary follicles. Small fluid-filled spaces become visible between the granulosa cells (fig.153). These spaces enlarge and fuse to form the follicular antrum.

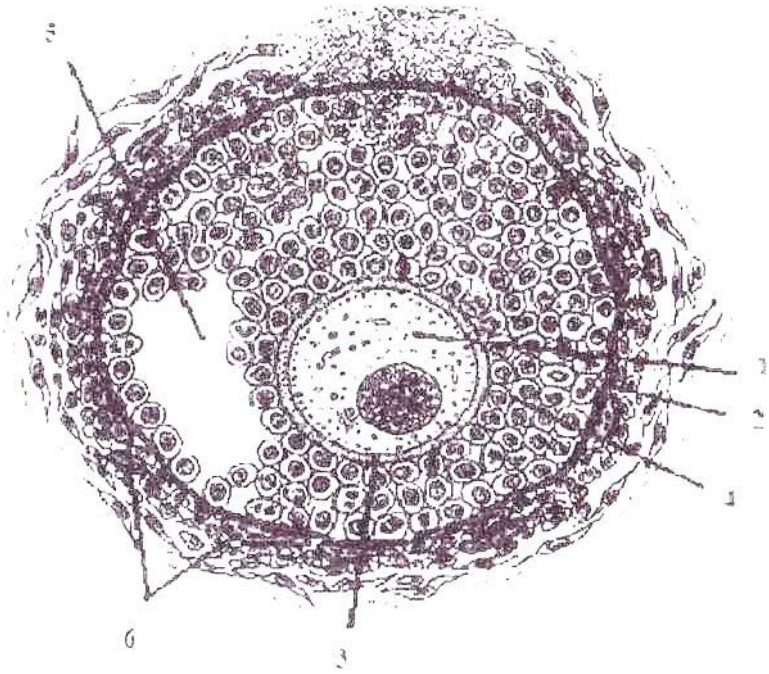


Figure 153. Secondary follicle. 1 - oocyte, 2 - basal lamina, 3 - zona pellucida, 4 - granulosa cells, 5 - antrum, 6 - blood vessels (from Ross M.H., 2003)

The oocyte is now located eccentric in the follicle, and is surrounded by granulosa cells. Theca folliculi further differentiates into two layers.

- **Theca interna** is layer of steroid-producing secretory cells. These cells have luteinizing hormone (LH) receptors. In response to LH stimulation, they secrete androgens that are the precursors of estrogens.
- **Theca externa** is the outer layer of connective tissue

Mature (tertiary, preovulatory, Graafian) follicle (fig.154) increases further in size (is about 2,5 cm in diameter) and bulges from the surface of the ovary. Oocyte adheres to cumulus oophorus.

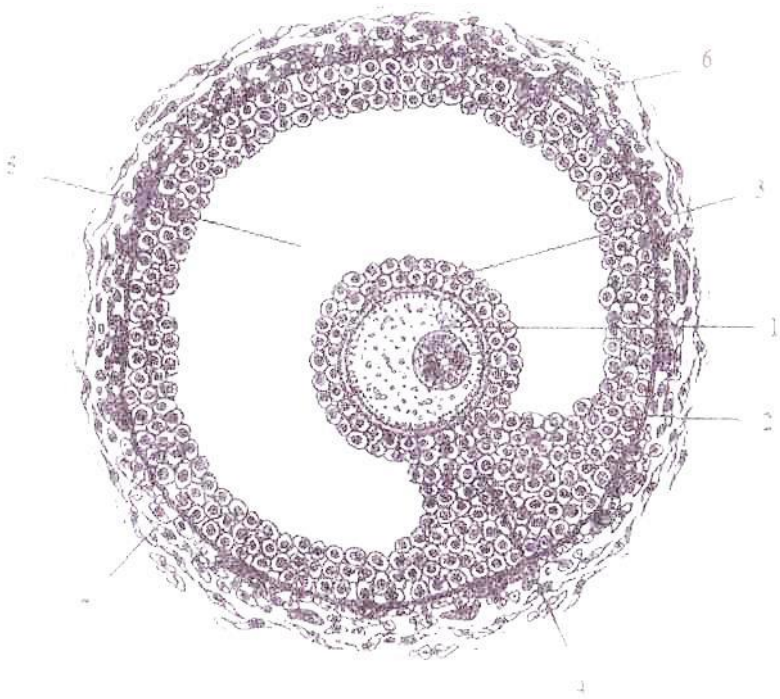


Figure 154. Mature follicle. 1 - oocyte, 2 - basal lamina, 3 - cells that will become corona radiata after ovulation, 4 - cumulus oophorus, 5 - antrum filled with follicular fluid, 6 - granulosa cells, 7 - theca tblliculi (from Ross M.H.,).

Ovulation.Ovulation is a hormone-mediated (LH of the pituitary gland) process of liberation of the secondary oocyte by the rupture of Graafian follicle into the peritoneal cavity. Ovulation takes place in the middle of the menstrual cycle, on the 14th day of a 28-day cycle.

Corpus luteum After ovulation, the follicular wall, composed of the granulosa and theca cells, is transformed into the temporary endocrine gland called corpus luteum {luteal gland).

Development of the corpus luteum/ Development of the corpus luteum includes **4 stages**:

I. The cells of the granulosa and theca interna proliferate; blood vessels from theca interna rapidly grow into the granulosa layer.

II. The cells of the granulosa and theca interna (luteal cells) increase in size and become filled with yellow pigment lutein, and demonstrate features associated with steroid-secreting cells (abundant sER and mitochondria).

III. Cells of corpus luteum secrete female sexual hormones:

1) granulosa lutein cells, derived from the granulosa cells, secrete progesterone;

2) theca lutein cells, derived from the cells of theca interna layer, secrete androgens and estrogens. These hormones stimulate the growth and secretory activity of the endometrium, to prepare it to the implantation of the zygote.

IV. Degeneration and involution of the corpus luteum after pregnancy or menstruation. White scar, the corpus albicans, is formed. It slowly disappears over a period of several months.

Types of the corpus luteum

1) If the oocyte is not fertilized, the corpus luteum stops secreting progesterone and remains only for 14 days; in this case it is called the menstrual corpus luteum.

2) If the oocyte is fertilized and implantation occurs, the trophoblast cells of the blastocyst secrete the hormone human chorionic gonadotrophin (hCG). Human chorionic gonadotrophin signals the corpus luteum to continue progesterone secretion, thereby maintaining the endometrium of the uterus and providing an area rich in blood vessels in which the zygote(s) can develop. In this case the corpus luteum is called the corpus luteum graviditatis. Corpus luteum graviditatis measures 5 cm. Its function begins to decline after 8 weeks of pregnancy, although it persists throughout pregnancy.

Ovarian follicular atresia. Most ovarian follicles are lost by atresia mediated by apoptosis of granulosa cells on any stage of maturation. The cells of the theca interna proliferate to form the interstitial glands, also called the corpora atretica. These glands secrete estrogens.

Ovarian cycle.During each menstrual cycle, the ovary undergoes cyclic changes that involve two phases (fig.155):

- **follicular phase**
- **luteal phase**

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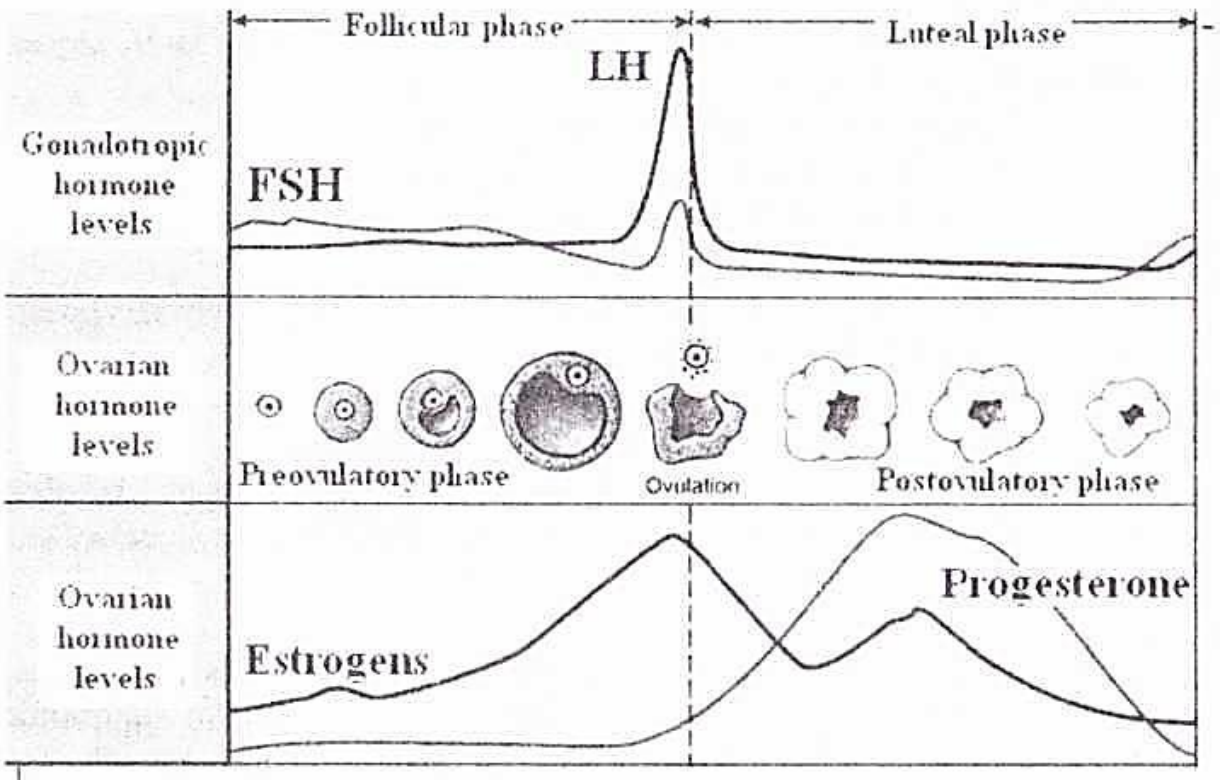


Figure 155. Relitionship of events that occur in ovarian cycle.

Ovulation occurs between two phases. The follicular phase begins with the development of primary follicles under the influence of FSH and TH. FSH stimulates the granulosa and thecai cells, which begin to secrete estrogens. Late in the follicular phase, before ovulation, progesterone levels begin to rise under the influence of LH. Ovulation is induced by a surge in the LH level, which occur with a smaller increase in the FSH level. The luteal phase begins after ovulation, as the granulosa and thecal cells of the ruptured follicle undergo transformation to form the corpus luteum. Estrogens and large amounts of progesterone are secreted by the corpus luteum.

Oogenesis. Oogenesis is the process of differentiation of the oocytes(fig.156)

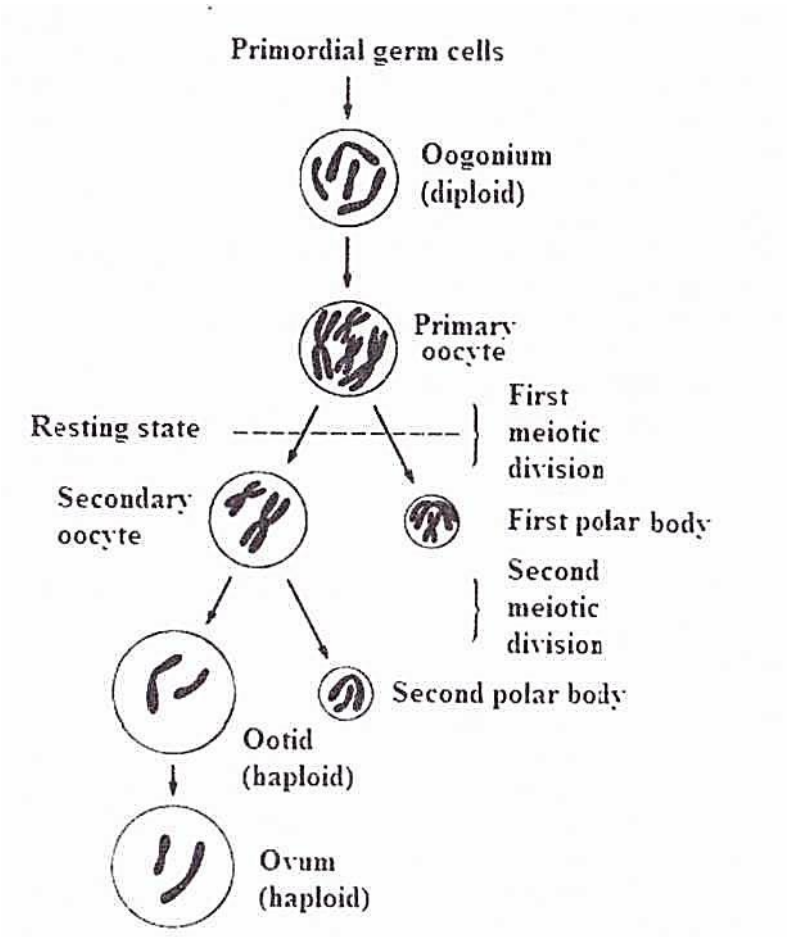
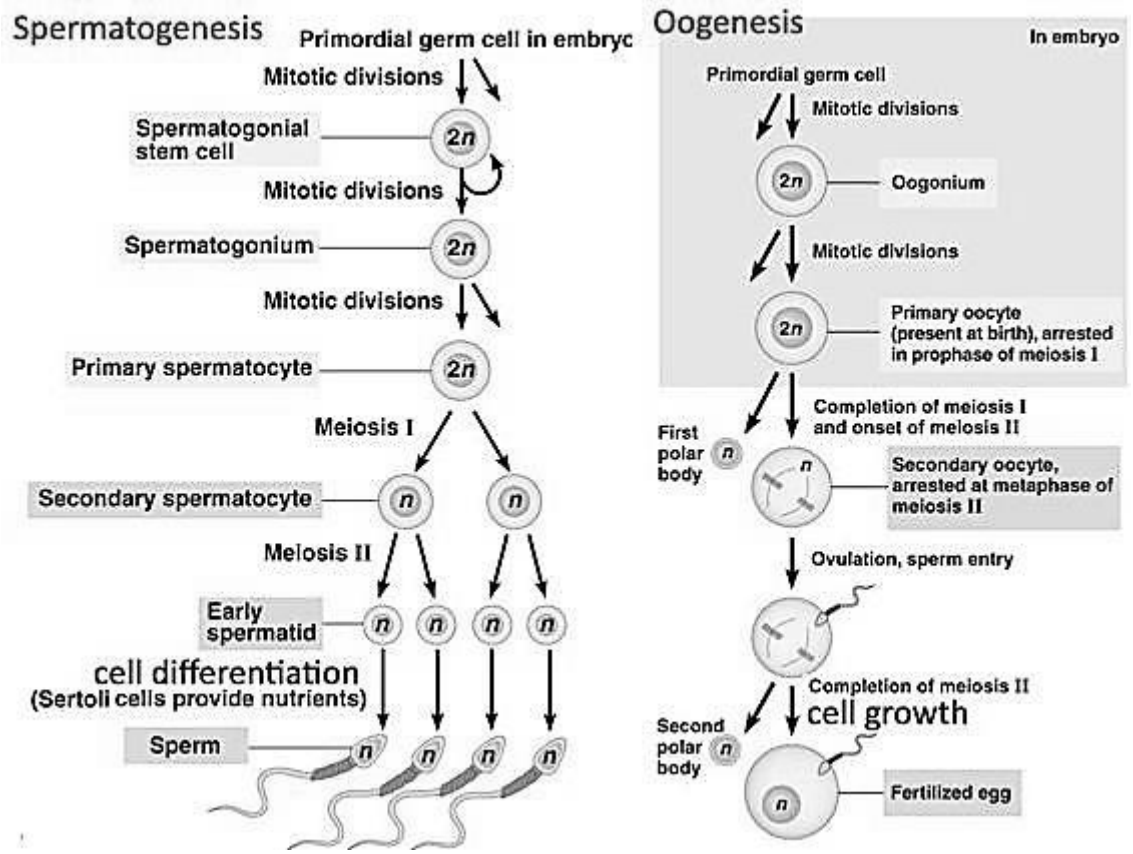


Figure 156. Schematic diagram of oogenesis.

The oogonia proliferate by mitosis during the fetal life in the cortex of the ovary and are used throughout the life of a woman. Each oogonium enlarges to form a primary oocyte (46 chromosomes, 4N DNA). Primary oocyte within the primordial follicle begins the first meiotic division in the embryo, but this process is arrested at the diplotene stage of meiotic prophase. Primary oocytes remain arrested in the first meiotic prophase for 12-50 years. The first meiotic division is completed in the mature follicle, and one daughter cell (secondary oocyte (23 chromosomes, 2N DNA)) receives most of the cytoplasm. Other daughter cell (first

polar body) receives a minimal amount of cytoplasm. The secondary oocyte begins the second meiotic division, the daughter cells being again unequal. The large daughter cell is the mature ovum (23 chromosomes, IN DNA). The smaller daughter cell is the second polar body. This second division does not occur unless fertilization of the secondary oocyte by a sperm occurs.



Oviducts (uterine or Fallopian tubes). The uterine tubes are paired muscular tubes about 12 cm long, which connect the peritoneal cavity with the cavity of uterus. They receive and transport ovum to the uterus and provide the necessary environment for fertilization and initial development of the zygote.

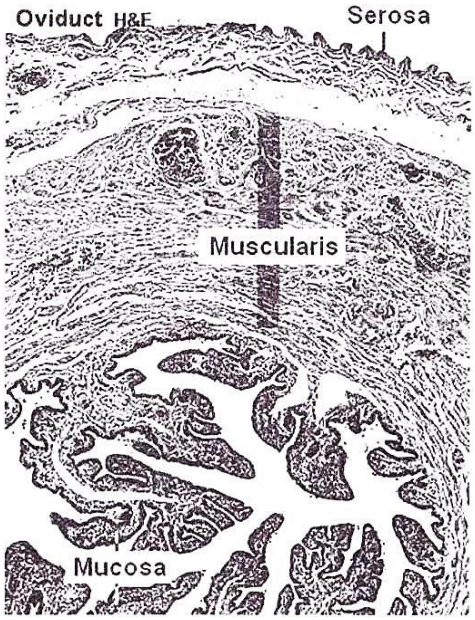


Figure 157. Photomicrograph of a human uterine tube.

The wall of the oviduct is composed of three layers (fig.157):

- **mucosa,**
- **muscularis,**
- **serosa**

I. Mucosa has longitudinal folds and consists of:
1) **epithelium** is simple columnar and contains two types of cells:
- **ciliated** cells, wave of the cilia of these cells is directed toward the uterus;
- **nonciliated**, secretory, peg cells which produce the fluid that provides nutrition for the ovum.
2) lamina propria is composed of loose connective tissue;
II. Muscularis consists of 2 sublayers of smooth muscle tissue (outerlongitudinal and inner-circular);
III. Serosa is covered by mesothelium.

Uterus.The uterus is a pear-shaped organ that receives the morula from the uterine tube. **The wall of the uterus is formed of 3 layers:**
I. mucosa (endometrium),
II. muscularis (myometruim)
III. serosa (perimetrium)
Endometrium consists of:
1) simple columnar epithelium that contains ciliated and secretory cells;
2) lamina propria contains simple tubular glands (the uterine glands);
Endometrium can be divided into two zones:
1) basal layer is not sloughed off during menstruation but functions as a regenerative zone for the functional layer after its rejection; is supplied by straight arteries.
2) functional layer is the luminal part of the endometrium; it is sloughed off during every menstruation and it is the site of cyclic changes in the endometrium; is supplied by spiral arteries.
Myometrium is composed of 3 layers of smooth muscle tissue. The middle layer contains numerous large blood vessels and is called stratum vascularis. The inner and outer layers contain smooth muscle bundles oriented parallel to the long axis of the uterus.
Outer layer is either serosa (perimetrium, the serous membrane enveloping the fundus and ventral and dorsal surfaces of the uterus) or adventitia consisting loose connective tissue. **Parametrium** is the loose connective tissue around the uterus.
Menstrual (uterine) cycle. The menstrual (uterine) cycle is a continuum of developmental stages in the functional layer of the endometrium, normally repeats every 28 days. Menstrual cycle has 3 successive phases (fig.158):

I. Menstrual
II. Proliferative
III. Secretory

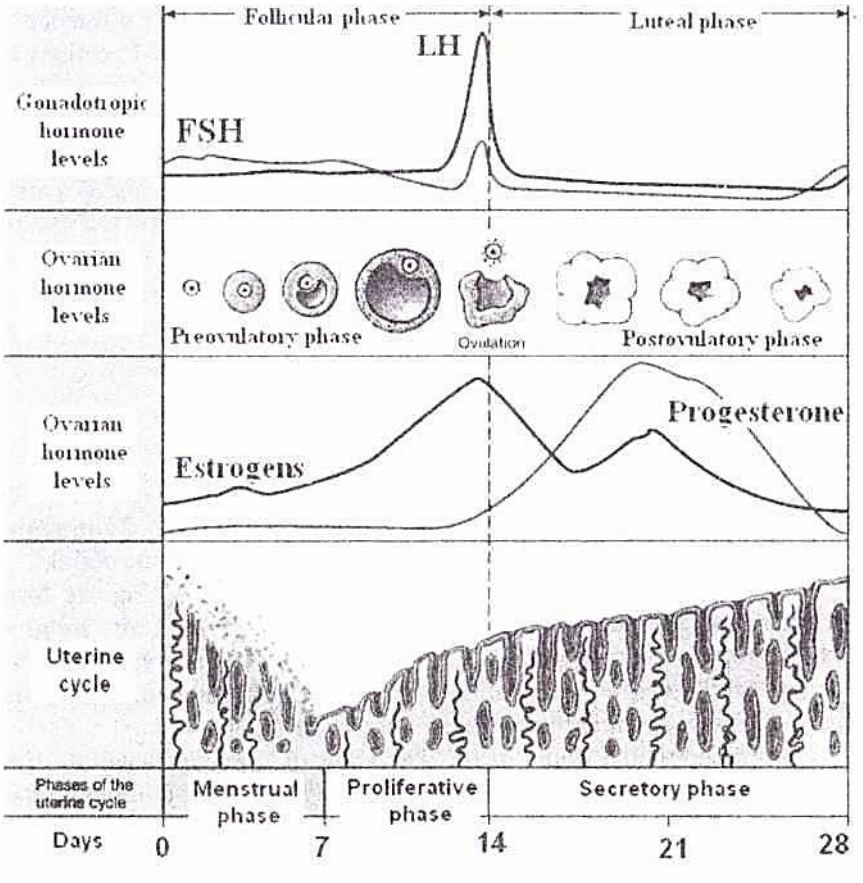


Figure 158. Relationship of events that occur in ovarian and menstrual cycles

Menstrual phase (1-4 days) At the end of the secretory phase ovarian hormone levels rapidly decrease; the walls of the spiral arteries contract, closing off the blood flow and producing ischemia (local anemia), which results in death (necrosis) of their walls and of the functional layer of the endometrium.At this time, blood vessels above the constrictions rupture, and bleeding begins. The average blood loss in the menstrual phase is 35 to 50 mL. Only the basal layer containing basal parts of uterine glands are left. Proliferation of the gland cells and their migration to the surface initiate the proliferative phase.

Proliferative phase (5-14 days) is initiated under the influence of estrogens. The lost epithelium is regenerated from the basal portions of the uterine glands. At the end of the proliferative phase the endometrium is 2-3 mm thick, the glands are straight tubules with narrow lumens.

Secretory phase (15-28 days) of the menstrual cycle is regulated by progesterone of the corpus luteum. The glands become highly coiled and secrete glycoproteins that will be the major source of embryonic nutrition before implantation occurs. In this phase, the endometrium reaches its maximum thickness (5mm) as a result of the accumulation of secretions and the edema of the stroma. The last few days of this period is called ischemic phase.

Mammary glands (breasts) (fig.159)

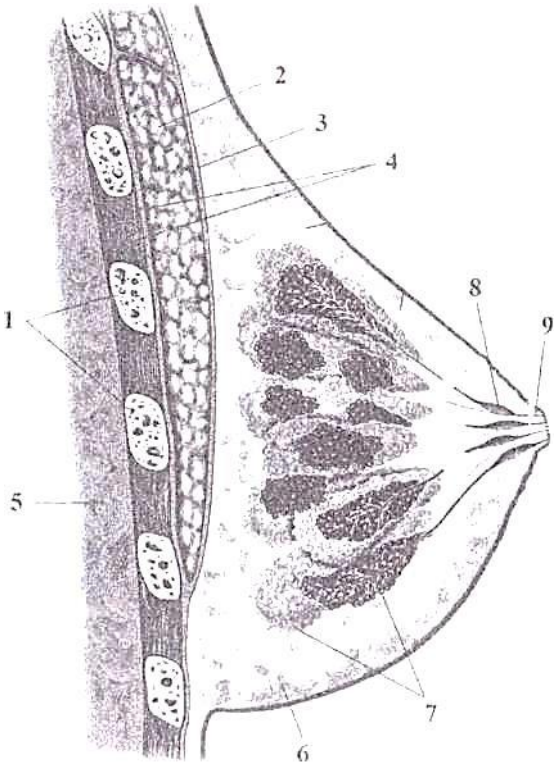


Figure 159. Schematic diagram of the human mammary gland. 1 - ribs, 2 - pectoralis major muscle, 3 - pectoral fascia 4 - intercostal muscles, 5 - lung, 6 - fat, 7 — gland lobules, 8 - lactiferous sinus, 9 - lactiferous duc

The mammary glands are modified apocrine sweat glands of the skin. The inactive adult mammary gland is composed of 15-25 irregular lobes separated by fibrous band of' interlobar connective tissue and fat. Each lobe contains an individual gland. The lobes radiate from the mammary papilla, or nipple. The lobes are subdivided into lobules. The excretory duct of each lobe, also called lactiferous duct, has opening on the nipple. Beneath the areola each has a dilated portion, the lactiferous sinus, which functions as a reservoir for the milk. The epithelial lining of the duct shows a gradual transition from single layer of columnar or cuboidal cells to two layered epithelium and finally to stratified squamous nonkeratinized epithelium. Branches of the lactiferous duct are lined with a simple cuboidal epithelium. The lactiferous duct has a two layered epithelium - basal cells are cuboidal whereas the superficial cells are columnar. Lactiferous sinuses are lined by stratified squamous nonkeratinized epithelium. The lobules contain the secretory units (alveoli), which are lined by a cuboidal or columnar epithelium (secreting cells - lactocytes) (fig.160). The myoepithelial cells surround the base of the alveolar secretory cells and the bases of the cells of the larger ducts, causing them to contract and eject the milk from the alveoli. Secreting cells contain abundant granular endoplasmic reticulum, mitochondria, Golgi apparatus, lysosomes. Milk proteins aresecreted by merocrine secretion, milk lipids are secreted by apocrine secretion. Hormonal regulation of the mammary gland The initial growth of the mammary glands at puberty occurs under the influence of estrogens and progesterone produced by maturing ovary. Lactation is under neurohormona! control of the adenohypophysis (prolactin) and hypothalamus

(oxytocin). Production of milk is stimulated by prolactin. Oxytocin stimulates the myoepithelial cells.

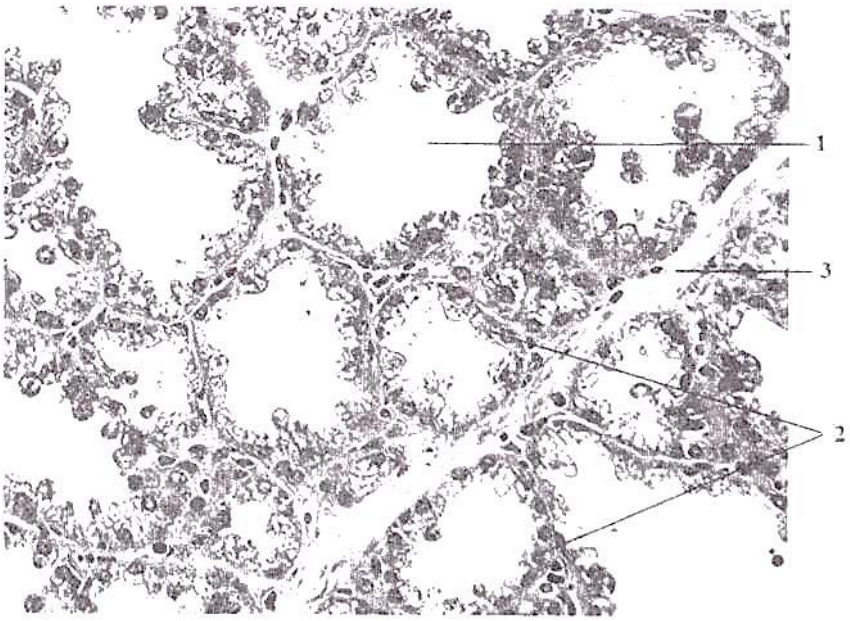


Figure 160. Photomicrograph of a lactating mammary gland of a young woman. 1 - secretory units (alveoli), 2 - lactocytes, 3 - interlobar connective

Vagina. The wall of the vagina from the ***lumen out***wards consists **firstly** of ***a mucosa*** of
1.**non-keratinized stratified squamous epithelium** with an underlying
2. **lamina propria of connective tissue,**
secondly *(*muscular) a layer ***of smooth muscle with*** bundles of circular fibers internal to longitudinal fibers, and thirdly an outer layer of connective tissue called the ***adventitia.*** Some texts list four layers by counting the two sublayers of the mucosa (epithelium and lamina propria) separately. The lamina propria is rich in blood vessels and lymphatic channels. The **muscular layer** is composed of smooth muscle fibers, with an outer layer of longitudinal muscle, an inner layer of circular muscle, and oblique muscle fibers between. The outer layer, **the adventitia**, is a thin dense layer of connective tissue, and it blends with loose connective tissue containing blood vessels**, lymphatic vessel s**and nerve fibers that is present between the pelvic organs.

Folds of mucosa (or vaginal rugae) are shown in the front third of a vagina.
A normal cervix of an adult as seen through the vagina (per vaginam or PV) using a bivalved vaginal speculum. The blades of the speculum are above and below and stretched vaginal walls are seen on the left and right.
The mucosa forms folds or rugae, which are more prominent in the caudal third of the vagina; they appear as transverse ridges and their function is to provide the vagina with increased surface area for extension and stretching. Where the vaginal lumen surrounds the cervix of the uterus, it is divided into four continuous regions

or vaginal fornices; these are the anterior, posterior, right lateral, and left lateral fornices. The posterior fornix is deeper than the anterior fornix.[13] While the anterior and posterior walls are placed together, the lateral walls, especially their middle area, are relatively more rigid; because of this, the vagina has a H-shaped cross section. Behind, the upper one-fourth of the vagina is separated from the rectum by the recto-uterine pouch. Superficially, in front of the pubic bone, a cushion of fat called the mons pubis forms the uppermost part of the vulva.

Supporting the vagina are its upper third, middle third and lower third muscles and ligaments. The upper third are the levator ani muscles (transcervical, pubocervical) and the sacrocervical ligaments; these areas are also described as the cardinal ligaments laterally and uterosacral ligaments posterolaterally. The middle third of the vagina concerns the urogenital diaphragm (also described as the paracolpos and pelvic diaphragm). The lower third is the perineal body; it may be described as containing the perineal body, pelvic diaphragm and urogenital diaphragm.

The epithelial covering of the cervix is continuous with the epithelial lining of the vagina. The vaginal mucosa is absent of glands. The vaginal epithelium consists of three rather arbitrary layers of cells – superficial flat cells, intermediate cells and basal cells – and estrogen induces the intermediate and superficial cells to fill with glycogen. The superficial cellsexfoliate continuously and basal cells replace them. Under the influence of maternal estrogen, newborn females have a thick stratified squamous epithelium for two to four weeks after birth. After that, the epithelium remains thin with only a few layers of cells without glycogen until puberty, when the epithelium thickens and glycogen containing cells are formed again, under the influence of the girl's rising estrogen levels. Finally, the epithelium thins out during menopause onward and eventually ceases to contain glycogen, because of the lack of estrogen. In abnormal circumstances, such as inpelvic organ prolapse, the vaginal epithelium may be exposed becoming dry and keratinized.

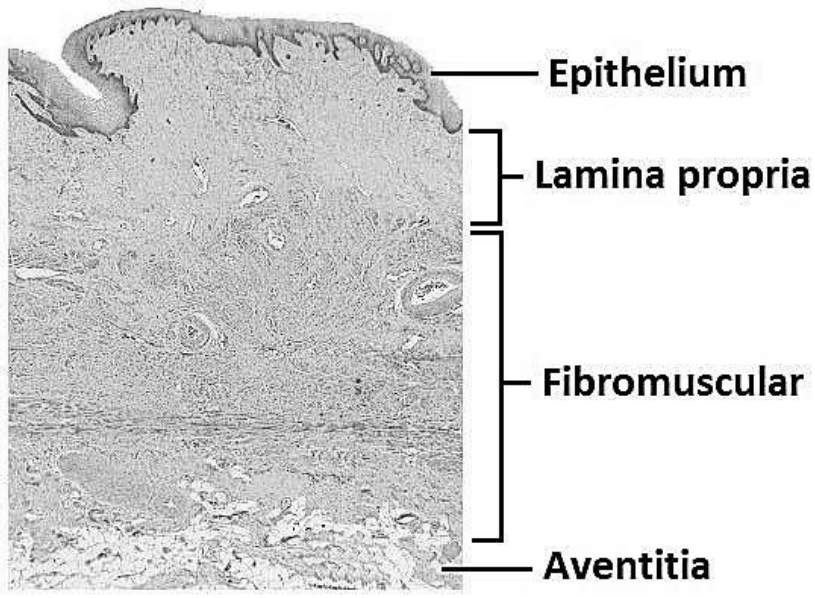
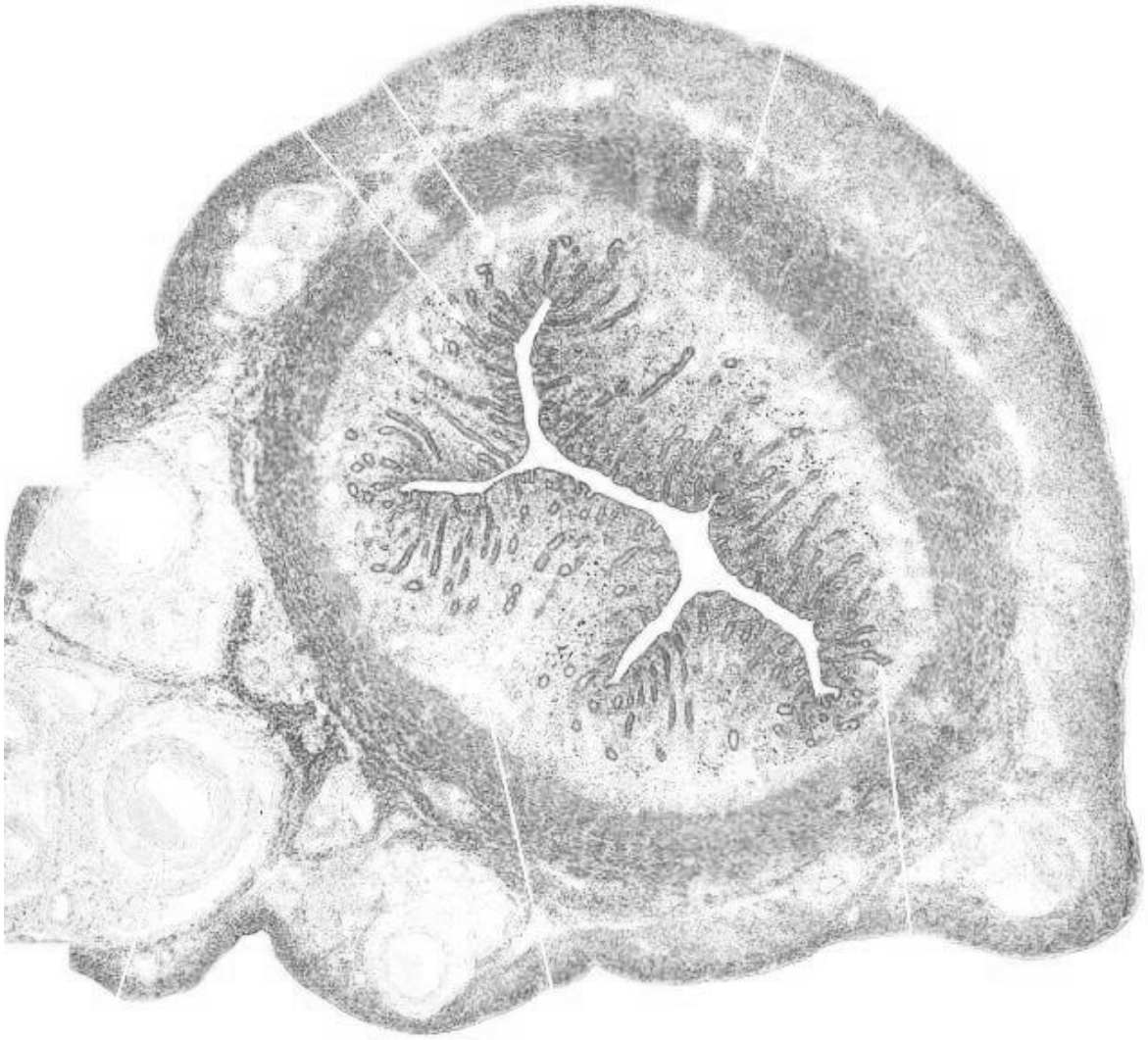


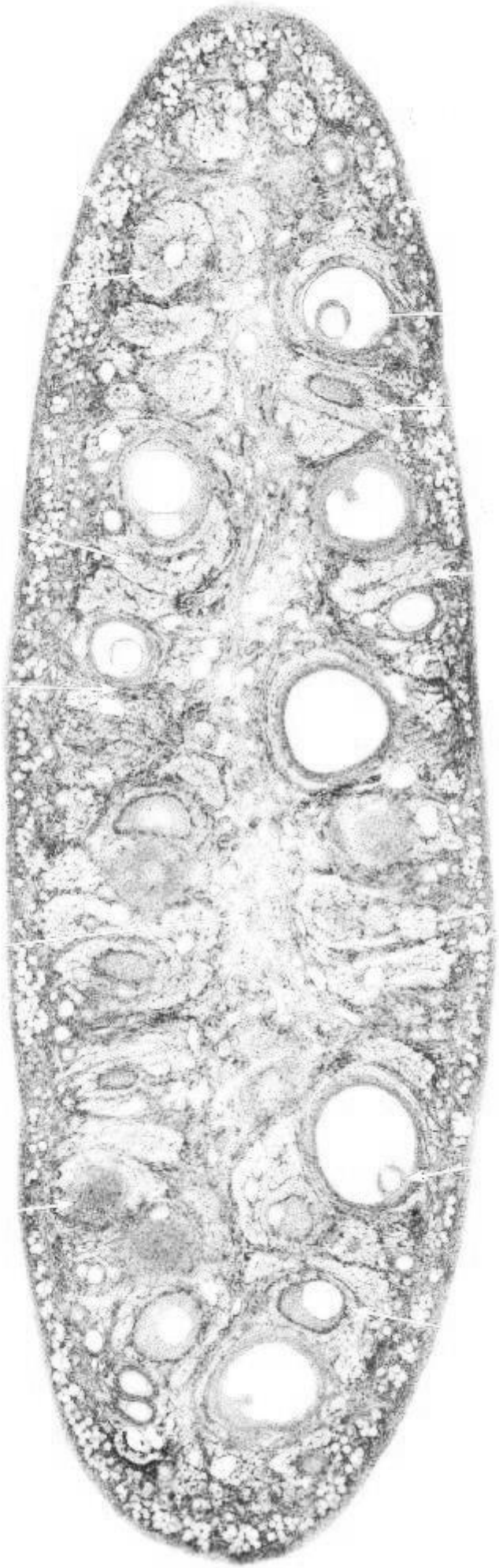
Figure 160. Vagine.

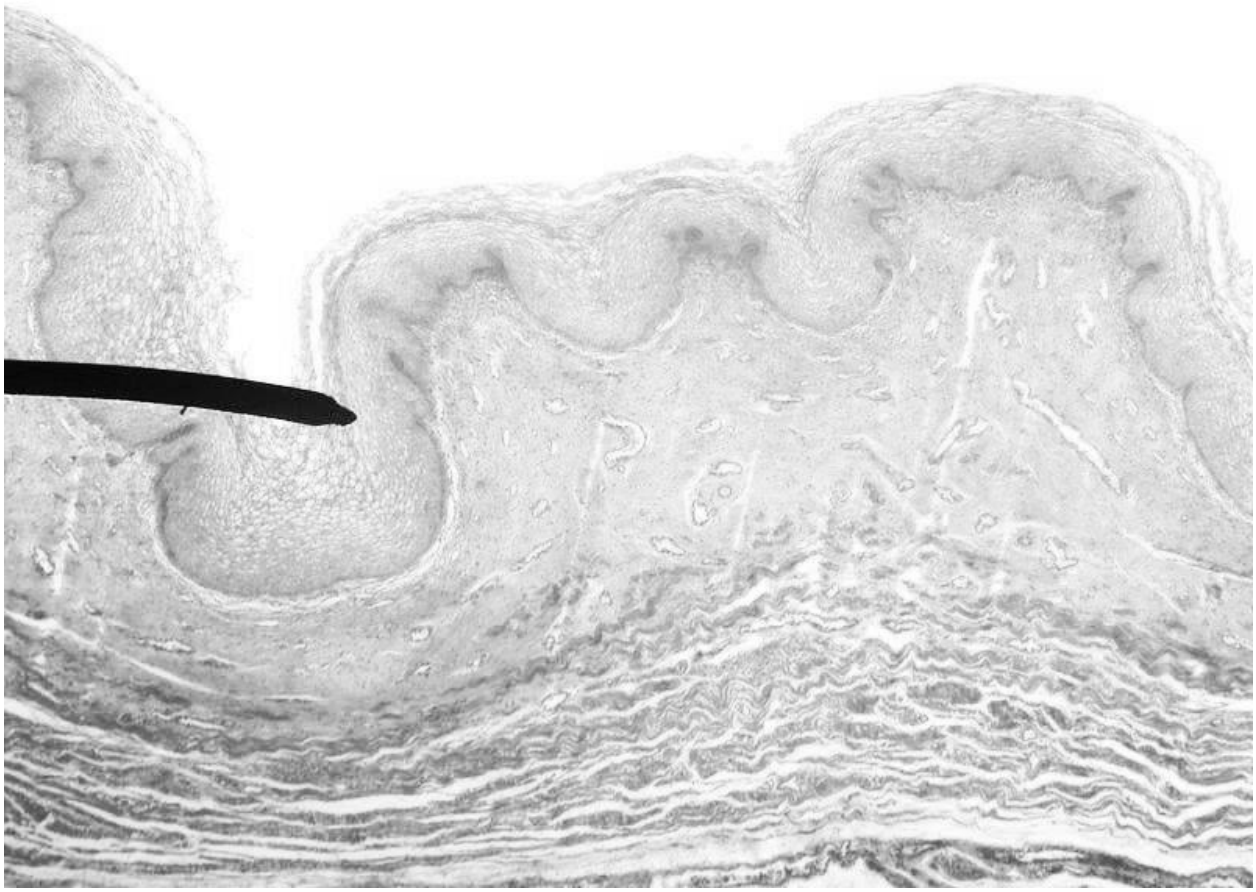
Practical lessons

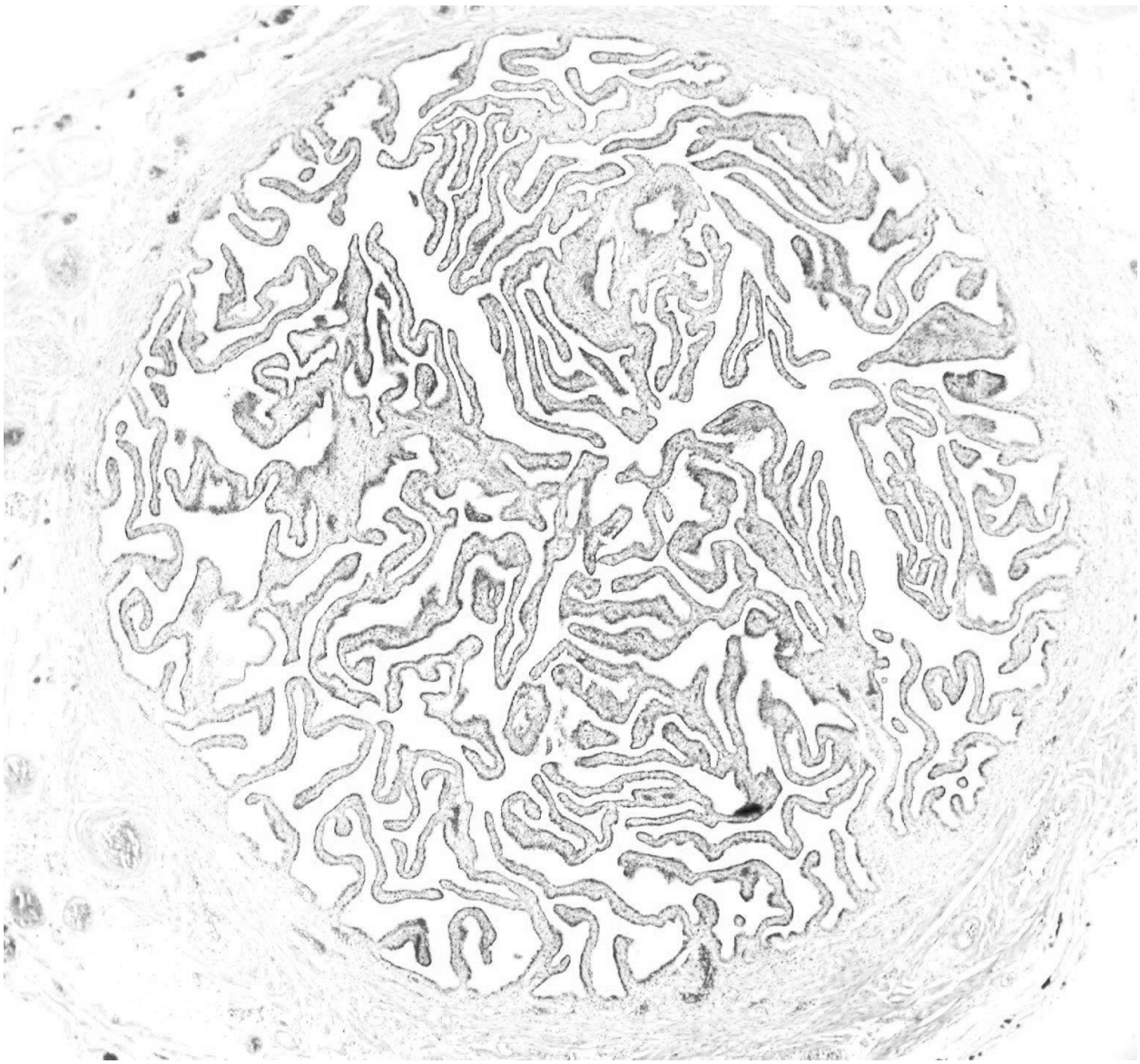
1.Ovary: structure and functions.
2.Oogenesis.
3. Uterus: structure and functions
4.Vagina. structure and functions
5.Menstrual (uterine) cycle.
6.Mammary gland: structure and functions. Lactation, nervous and endocrine regulation.

Paint and mark basic histological structure









Signature of teacher_____

ENDOCRINE SYSTEM

CENTRAL ENDOCRINE ORGAN. The endocrine system is a system of glands, each of which is ductless and secretes the hormones into the bloodstream to regulate many functions of an organism, including growth, development, and metabolism. The blood and lymph carry hormones to the target organs. **Hormones** are substances (chemical mediators) released from endocrine tissue into the blood that attach to target cells and allow communication among cells. The ability of a target cell to respond to a hormone depends on the presence of receptors, within the cell or on its plasma membrane, to which the hormone can bind.

Classification of the endocrine structural components

I. **Central regulatory formations of the endocrine system**:
hypothalamus,
hypophysis cerebri (pituitary gland),
pineal gland (epiphysis)

II. **Peripheral endocrine organs**:
thyroid gland,
parathyroid glands,
adrenal (suprarenal) glands

III. **Organs having endocrine and nonendocrine functions**:
gonads (testes, ovaries),
pancreas,
placenta

IV .**Isolated endocrine cells in the epithelium of the organs** of the respiratory passages, gastro-intestinal tract, urinary system ,
APUD cells,
isolated endocrine cells which secrete steroid and other hormones.

APUD cells constitute a group of the endocrine cells which have the common function of secreting low molecular weight polypeptide hormones. The name is derived from an abbreviation, referring to the following: Amine - for high amine content, Precursor Uptake - for high uptake of (amine) precursors, Decarboxylase - for high content of the enzyme amino acid decarboxylase (for conversion of precursors to amines).

Hypothalamus .The hypothalamus is a portion of the brain which is responsible for certain metabolic processes and other activities of the autonomic nervous system. It synthesizes and secretes certain neurohormones, often called hypothalamic-releasing hormones, and these in turn stimulate or inhibit the secretion of pituitary hormones. The hypothalamus controls body temperature, hunger, thirst, fatigue, sleep, and circadian cycles. The hypothalamus contains neurosecretory (magnocellular and parvocellular) nuclei. The **secretory neurons** (fig.161) of these nuclei have all characteristics of typical neurons, including the ability to product the neurohormones.

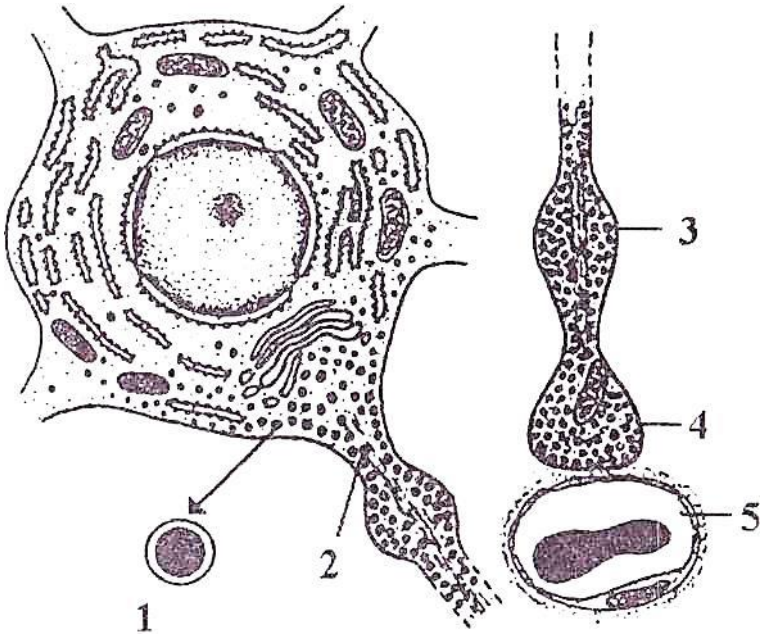


Figure 161. Schematic representation of the secretory neuron. 1 — neurosecretory granules, 2 - axon, 3 - accumulation (Herring body), 4 - axovasal synapse, 5 - blood capillary (from EuKoe B.JI., 1999)

Neurosecretory nuclei of hypothalamus depending on their sizes and functions are subdivided into magnocellular and parvocellular.

I. **Magnocellular nuclei (supraoptic and paraventricular**). The axons of neurosecretory cells of these nuclei forming hypothalamohypophyseal tract pass along the infundibular stalk and terminate in neurohypophysis as accumulations in relations to blood capillaries (flg.162). These accumulations are called Herring bodies. The neurosecretory cells of supraoptic nucleus secrete vasopressin also called antidiuretic hormone (ADH). The main effect of **vasopressin** is:

- to increase the permeability to water of the distal convoluted tubules and the collecting tubules of the kidney; as a result, water is absorbed by these tubules and urine becomes hypertonic;
- to contract smooth muscle tissue of small arteries and raises the blood pressure.

The neurosecretory cells ofparaventricular nuclei secrete oxytocin. **Oxytocin stimulates contraction of:**

- the smooth muscle tissue of the uterine wall during childbirth and
- the myoepithelial cells of alveoli of the mammary glands during the nursing

II. **Neurosecretory cells of the parvocellular nuclei** synthesize and secrete certain neurohormones, often called **hypothalamic-releasing hormones**, and these in turn stimulate or inhibit the secretion of pituitary hormones:

- **Thyrotropin-releasing hormone** (TRH) or thyroliberin stimulates the release of thyroid-stimulating hormone (TSH) and prolactin by the pars distalis of adenohypophysis; TRH is produced by the medial neurons of the paraventricular nucleus;

- **Gonadotropin-releasing** hormone (GnRH) or luliberin is responsible for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pars distalis of adenohypophysis; is secreted by the neurons of the arcuate nucleus in the mediobasal hypothalamus;
- **Growth hormone-releasing** hormone (GHRH) or somatocrinin stimulates cells in the pars distalis of adenohypophysis to secrete growth hormone (GH), GHRH is secreted by the neurons of the arcuate nucleus in the mediobasal hypothalamus;
- **Corticotropin-releasing** hormone (CRH) acts on cells in the pars distalis of adenohypophysis to release adrenocorticotropic hormone (ACTH); CRH is produced by parvocellular neuroendocrine cells (which are contained within the paraventricular nucleus) of the hypothalamus;
- **Somatostatin a**cts on the pars distalis of adenohypophysis to inhibit the release of growth hormone (GH) and thyroid-stimulating hormone (TSH): somatostatin is produced by neuroendocrine neurons of the periventricular nucleus of the hypothalamus;
- **Dopamine** acts on the pars distalis of adenohypophysis to inhibit the release of prolactin (PRL) from the pars distalis of adenohypophysis; is secreted by the neurons of the arcuate nucleus in the mediobasal hypothalamus.

Hormones of parvocellular nuclei are released at the median eminence from neurosecretory terminals of these neurons into the primary capillary plexus of the hypothalamo-hypophyseal portal system. I he portal system carries these hormones to the secondary plexus in the pars distalis of the pituitary, where they regulate hypophyseal functions.

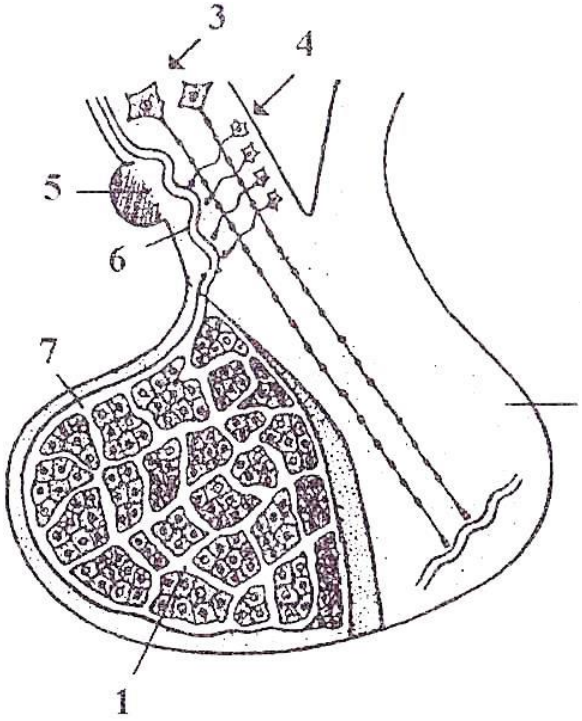


Figure 162. Hypothalamo-hypophyseal neurosecretory system. 1 - pars distalis of adenohypophysis, 2 - neurohypophysis, 3 - magnocellular nuclei, 4 - parvocellular

nuclei, 5 - optic chiasm, 6 - primary capillary network, 7 - secondary capillary network (from Ebixoa B.U., 1999).

Hypophysis (pituitary gland). The hypophysis (pituitary) is a pea-sized gland at the base of the brain which is located in the sella turcica of sphenoid bone (fig.20.3). The hypophysis consists of two parts (fig.163):

I. **Adenohypophysis (anterior pituitary**) which has three subdivisions:
1. pars distalis (anterior lobe);
2. pars tuberalis (intermediate lobe);
3. pars intermedia (tuberal lobe);
II**. Neurohypophysis (posterior pituitary**).
.**Adenohypophysis** 1. Pars distalis (75% of the mass of the hypophysis) coasists of branching cords of epithelial cells with capillaries between them (fig.164). Cells types of pars distalis have been described as
• chromophobic cells (chromophobes) and
• chromophilic cells (chromophils)

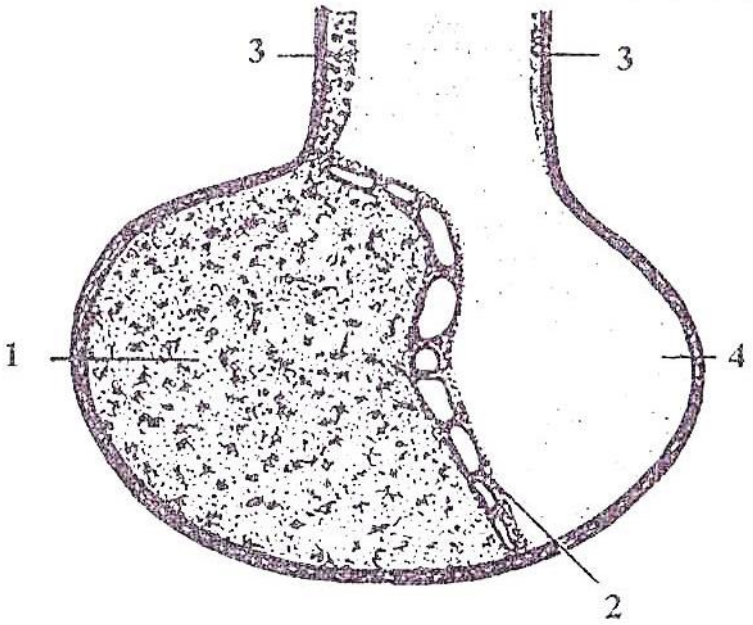


Figure 163. Schematic diagram of the hypophysis. 1 - pars distalis, 2 - pars intermedia, 3 - pars tuberalis, 4 - neurohypophysis (from Bmkob B.J7, 1999)

Chromophobes are:
• degranulated inactive resting cells capable of differentiation into a particular type of chromophils;
• undifferentiated cells;
• follicular cells which form a supporting network for the other cells.
Chromophils are called **acidophilic** (acidophils) or **basophilic** (basophils) **according** to their staining. **Acidophils** contain eosinophilic granules in their cytoplasm. **Subtypes of acidophils:**
1**) somatotropic cells** (somatotrophs) produce somatotropin (growth hormone), which acts on growth of long bones;

2**) mammotropic cells** (lactotropic cells, lac totrop Its) produce prolactin (mammotropic hormone), which promotes milk secretion.

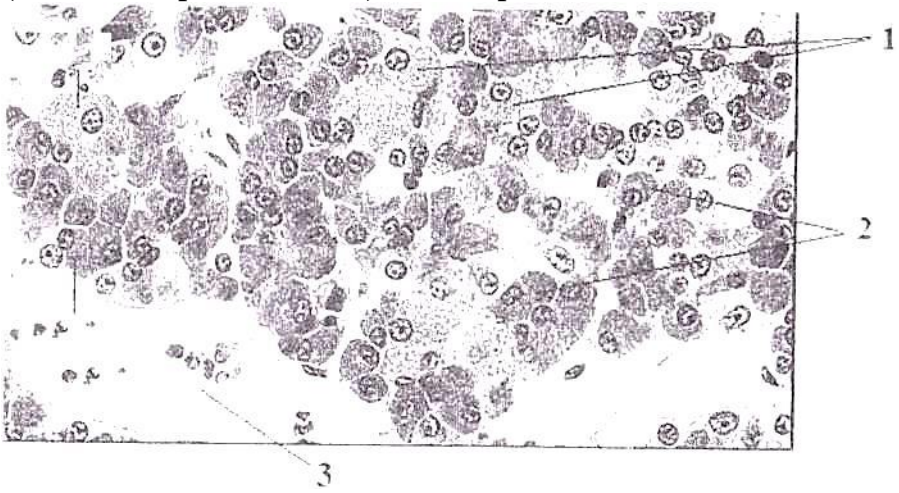


Figure 164. Photomicrograph of pars distalis of adenohypophysis. 1 - acidophils, 2 — basophils, 3 — blood capillary

Basophils contain small basophilic granules in their cytoplasm**. Subtypes of basophils:**

1) thyrotropic cells (thyrotrophs) produce thyrotropic hormone (thyrotropin), which stimulates thyroid hormone synthesis;

2**) gonadotropic** cells (gonadotrophs) produce:

- **follicle-stimulating** hormone (FSH), which promotes ovarian follicle development and estrogen secretion in female and stimulates spermatogenesis in male;
- **luteinizing hormone** (LH), which promotes ovarian follicle maturation, ovulation and progesterone secretion in female, androgen secretion in male,

3) **corticotropic cells** (corticotrophs) produce adrenocorticotropic hormone (ACTH), which stimulates secretion of adrenal cortex hormones.

Pars tuberalis surrounds the infundibulum of the neurohypophysis. Most of the cells of the pars tuberalis produce **gonadotropin**s (FSH and LH).

Pars intermedia forms a thin layer between the pars distalis and the neurohypophysis. It contains small ceils, which produce:

- **melanocyte-stimulating** hormone (MSH), which stimulates production of melanin by melanocytes;
- **lipotropin** or lipotropic hormone (LPH), which stimulates metabolism of fats.

Neurohypophysis. Neurohypophysis (fig.165) **consists of:**

- unmyelinated axons and dilated axon endings of secretory neurons from supraoptic and paraventricular nuclei of the hypothalamus; these axons form hypothalamo-hypophyseal tract, pass along the in infundibular stalk and terminate in the neurohypophysis as dilated terminal parts (Herring bodies) in relation to fenestrated blood capillaries; hormones vasopressin and oxytocin produced by these nuclei migrate along the axons in the neurohypophysis;

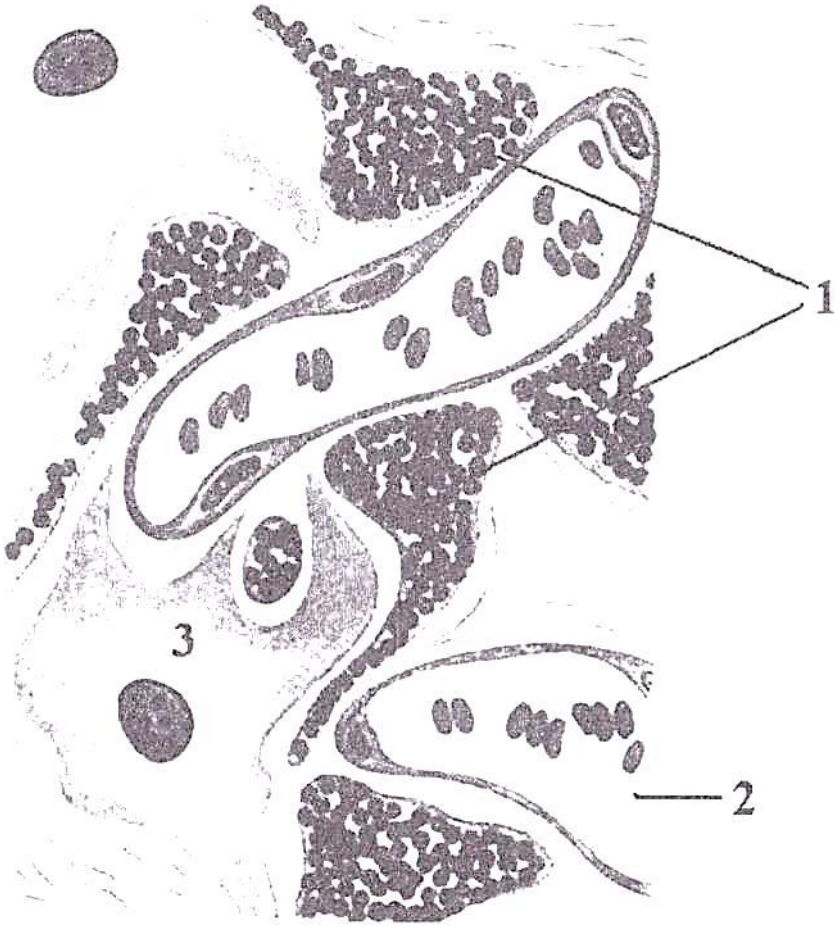


Figure 165. Schematic diagram of structure of neurohypophysis. 1 - Herring bodies, 2 - fenestrated blood capillary, 3 –pituicyte

- **fenestrated blood capillaries**;
- **pituicytes** are specific type of highly branched **glial cells**; their main function is supporting

Development of the hypophysis (fig.166) Adenohypophysis arises from an invagination from the ectodermal roof of primitive mouth cavity and forms Rath he's pouch. Neurohypophysis is neuro-ectodermal in origin and arises as an evagination from the floor of the diencephalon.

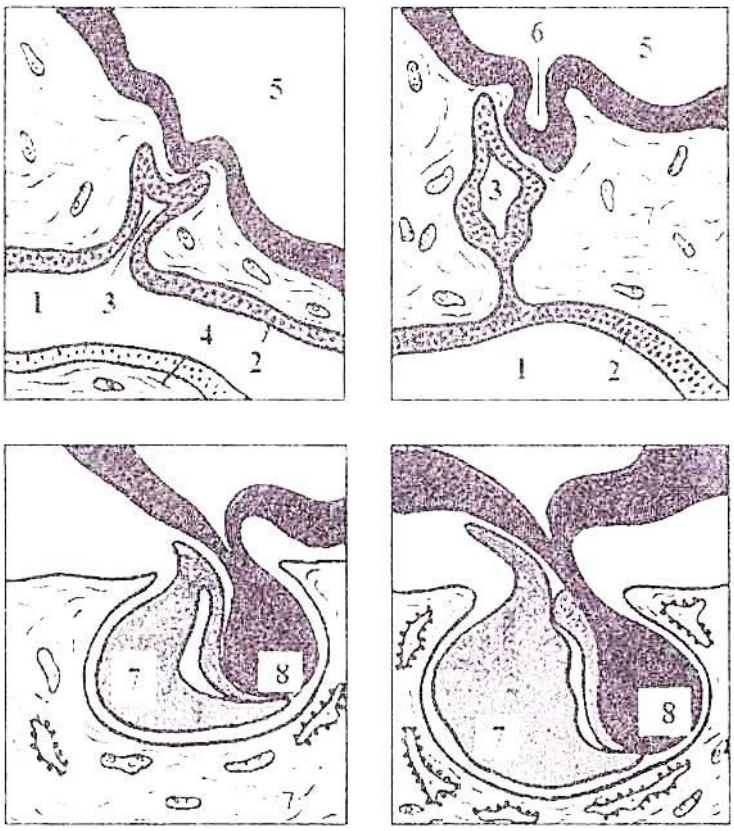


Figure 166. Development of the hypophysis. 1 — oral cavity, 2 — ectodermal epithelium of the oral cavity, 3 — Rathke's pouch, 4 — tongue, 5 — cavity of third ventricle, 6 - evagination of the diencephalon 7 - adenohypophysis, 8 — neurohypophysis.

Pineal gland (epiphysis cerebri or pineal body). The pineal gland is a small conical body, is evagination from the posterior part of the roof of the third ventricle of the brain. Connective tissue septa penetrate the pineal tissue and divide the organ into the irregular lobules. **The parenchyma of the pineal lobule consists of 2 types of cells:**

- **Pinealocytes** (90% of pineal cells), which have basophilic cytoplasm with large irregular or lobate nuclei; long highly-branched processes with terminal buds that end in relation to the wall of capillaries or in relation to the ependyma of the third ventricle. These cells produce melatonin and its precursor, serotonin.
- **Interstitial** (pineal astrocytes) (5% of pineal cells) are a specific type of neuroglial cells with elongated nuclei. These cells separate the pinealocytes from one another.

Pineal gland may contain **basophilic bodies** (pineal sand, pineal concretions) consisting of concentric layers of calcium and magnesium phosphate within an organic matrix. Appearance of concretions is the normal phenomenon which first registers in childhood; with age their amount and sizes is increased. **Histophysiology of the pineal gland**. The pineal gland is photosensitive organ and is an important regulator of day/night cycle (circadian rhythms) and seasonal biorhythms. It obtains information about light and dark cycles from

retina via retinothalamic tract, which connects in the suprachiasmatic nucleus with sympathetic neural tract travelling into pineal gland. During the day, light impulses inhibit the production of the major pineal gland hormone, melatonin. Plasma level of melatonin increases during darkness and decreases during light. In humans, these circadian changes of melatonin play an important role in regulation of daily body rhythms. The pineal gland plays a role in altering emotional responses to reduced day length during winter in temperate and subarctic zones (seasonal affective disorders). The pineal secretion promotes rhythmic changes in the secretary activity of the gonads and other organs.

Melatonin suppresses production of gonadotrophin releasing hormone by the hypothalamus, thus suppressing pituitary gonadotrophin secretion and activation of gonadal growth and hormonal secretion. At children with tumours, destroying an epiphysis, premature pubescence develops often.

PERIPHERAL ENDOCRINE ORGANS .

Thyroid gland. The thyroid gland is one of the largest endocrine glands in the body. The thyroid gland is derived from the cephalic portion of the alimentary canal (endoderm). **Function of the thyroid gland is to produce the hormones**:

- thyroid hormones which stimulate the rate of metabolism and are necessary for normal growth and development (cells of the brain are a major target for the thyroid hormones T3 and T4 ; thyroid hormones play a particularly crucial role in brain maturation during fetal development): • tetraiodothyronine or thyroxin (T4), which contains four atoms of iodine; • triiodothyronine (T3), which contains three atoms of iodine;
- calcitonin, which main effect is to lower blood calcium levels by inhibiting bone resorption.

Structure of the thyroid gland.The thyroid gland, located in the cervical region in front of the larynx, consists of two lobes united by an isthmus (fig.161). The thyroid gland is covered by connective tissue capsule. Septa extending into the gland from the capsule divide organ into lobules. The thyroid is an extremely vascularised organ, with an extensive blood capillary network.

Thyroid tissue is composed of follicles, which are structural units of the gland (fig.162). **Each follicle consists of a simple epithelium resting on a basal lamina.** The follicle has a cavity, which is filled by a **gelatinous substance** called colloid. Follicular epithelium consists of **two types of cells**:

- follicular cells,
- parafollicular cells

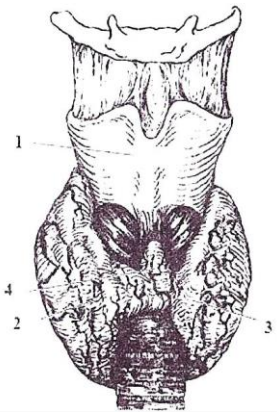


Figure 161. Position of the thyroid gland. 1 - larynx, 2 - right lobe, 3 - left lobe, 4 - isthmus

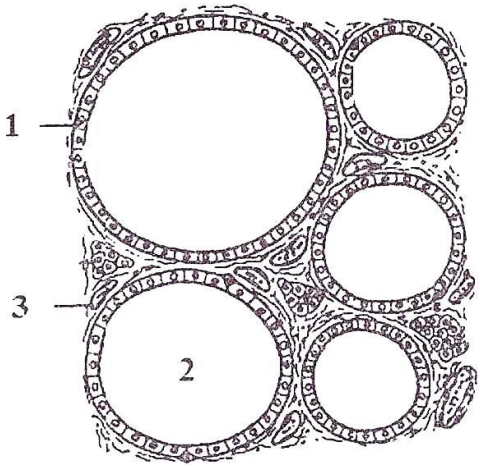


Figure 162. Schematic diagram of structure of the follicles of thyroid gland. 1 - follicular cells, 2 - colloid, 3 - blood capillary

Ultrastructure of follicular cells. Round nucleus of the follicular cell is in the center of the cell. The basal part of the cell is rich in rough endoplasmic reticulum. The apical pole contains Golgi complex, abundant small secretory granules. The cell membrane of the apical pole has number of microvilli. Numerous lysosomes and some large phagosomes are found in this region. Mitochondria, ribosomes are distributed throughout in the cytoplasm.

The follicular cells vary in shape depending on the level of their activity. **Normally** (at an average level of activity) the follicular cells are **cuboidal**, and **colloid in the follicles is of moderate amount**. When the cells are inactive, they have squamous shape. When the cells are highly active they become **columnar and colloid is scanty**.

Secretory cycle of the follicular cells. The secretory cycle (fig.163) of the follicular cells consists of:

- phase of production of hormones
- phase of liberation of hormones.

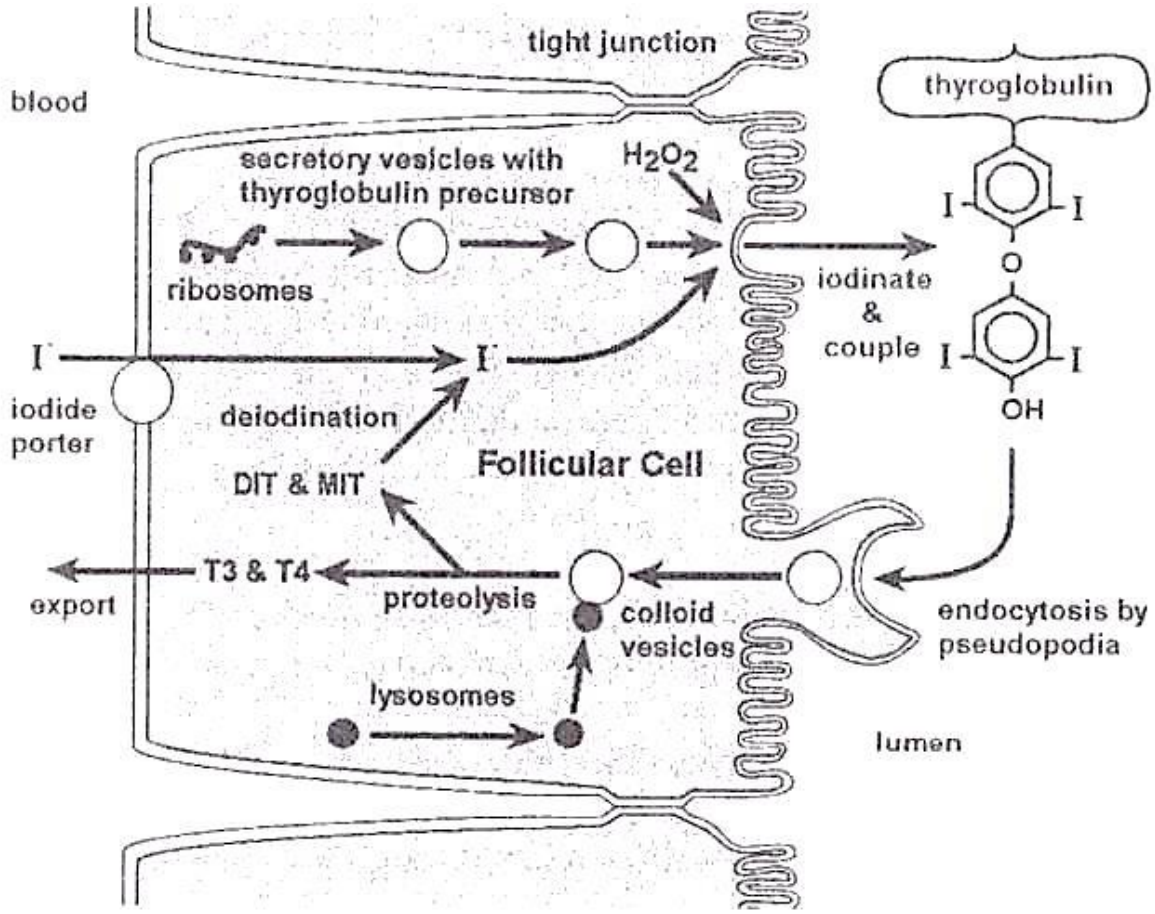


Figure 163. Schematic diagram of the secretory cycle of the follicular cells.

The phase of production of hormones includes:

1**) absorption of initial** products (aminoacid tyrosine, carbohydrates, water, iodide) from blood capillaries;
2**) synthesis of thyroglobulin** in the rough endoplasmic reticulum;
3) **non-enzymic iodination** and coupling together of tyrosine residues with the protein thyroglobulin; elemental iodine required for this reaction is produced by action of peroxidase on iodide ions and the reaction takes place on the apical surfaces of follicular cells;
4**) release of thyroglobulin** into the lumen of the follicle and formation of colloid.
The phase of liberation includes:
1) resorption of thyroglobulin from colloid by pinoeytosis;
2) hydrolysis of the thyroglobulin molecules by proteases in the lysosomes;
3) liberation of T3 and T4 into the cytoplasm;
4) liberation of T3 and T4 through the cell membrane into capillaries.
Thyroid gland regulation.The production of thyroxin and triiodothyronine is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary. The thyroid and thyrotrophes form a negative feedback loop: TSH production is

suppressed when the T4 levels are high. The TSH production is modulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus.

C-cells Another type of the cells, the parafollicular, or C, cells is found as part of the follicular epithelium or as isolated clusters between thyroid follicles These cells lie between the follicular cells and their basal lamina (fig.164). **Parafollicular cells** are larger and stain less intensely than follicular cells. They have well-developed rough endoplasmic reticulum, large Golgi complex, numerous mitochondria. Parafollicular cells produce the hormone calcitonin, whose main effect is to lower blood calcium levels by inhibiting bone resorption.

Secretion of calcitonin is triggered by an elevation in blood calcium concentration.

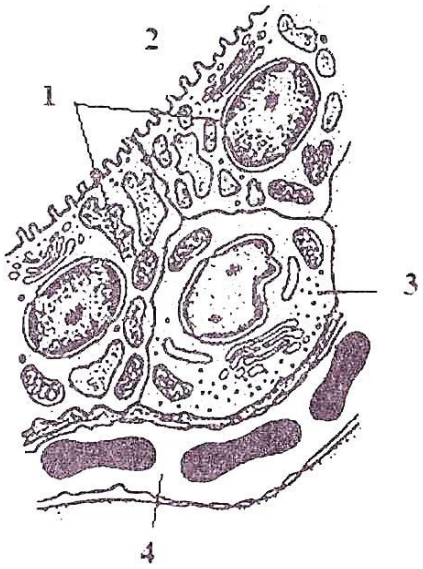


Figure 164. Schematic diagram of the thyroid gland cells. I - follicular cells, 2 - colloid, 3 — parafollicular cell, 4 - blood capillary

Parathyroid glands.The parathyroid glands are **4 small glands** (fig.165). They are behind the thyroid gland, one at each end of the upper and lower poles.

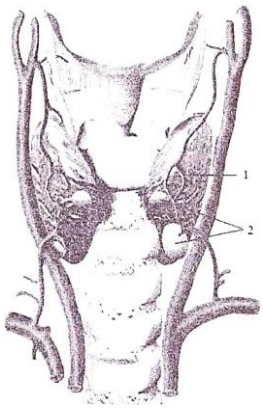


Figure 165. Position of the parathyroid glands. Back view. 1 - thyroid gland, 2 - parathyroid glands

These glands are situated under the capsule that covered the thyroid gland. Each parathyroid gland is covered by connective tissue capsule. The capsule sends septa into the gland. **The parenchyma of the parathyroid gland consists of two types of cells**:

1**) Chief cells** are most numerous. They have a pale-staining cytoplasm with vesicular nucleus. These cells produce parathyroid hormone (PTH) or parathormone. This hormone acts on the osteoclasts of bone (issue, increasing their number and activity, and thus promoting the absorption of the bone matrix and release of calcium into the blood.

2) **Oxyphil cells** are polygonal in shape and larger than chief cells. The function of these cells is unknown. Both the release of calcitonin by C cells in the thyroid gland and (lie release of parathyroid hormone are regulated by negative feedback from blood calcium concentrations.

Adrenal (suprarenal) glands. The adrenal glands are paired organs located near the upper pole of the kidneys. Each gland is covered by connective tissue capsule and has **2 parts** (fig.166, 167); Van outer cortex and an inner medulla.

Cortex and medulla differ in origin, structure, and functions. Adrenal cortex **Adrenal cortex is subdivided into 3 zones**:

1. outer zona glomerulosa;

2. middle zona fasciculata

3. inner zona reticularis.

1) . **Zona glomerulosa** consists of columnar cells arranged in rounded groups. The cells have light basophilic cytoplasm. Cells of zona glomerulosa secrete **mineralcorticoid hormones**, which function **is regulation of sodium and potassium homeostasis and water balance.** Principal hormone, **aldosterone**, acts on the distal tubules of the nephrons in the kidney, gastric mucosa, salivary and sweat glands to stimulate resorption of sodium, as well as to stimulate excretion of potassium by the kidneys. Aldosterone also participates in **blood pressure regulation.** Zona glomerulosa is under feedback control of the **renin-angiotensin-aldosteron system.**

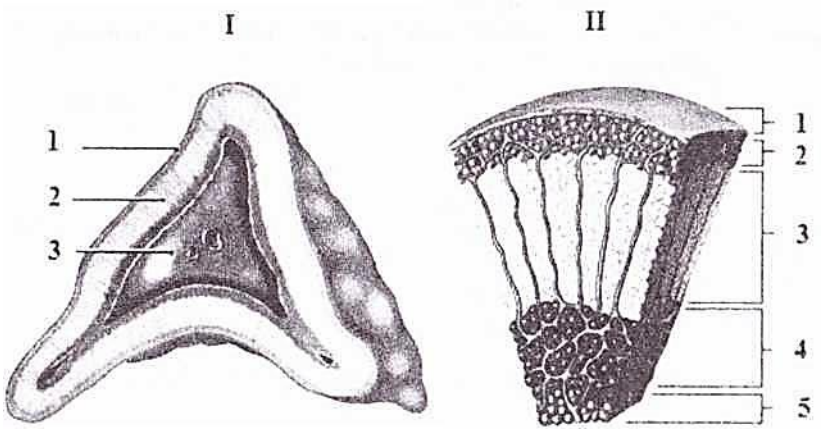


Figure 166. Schematic diagram of the adrenal gland. Transverse section:] - capsule, 2 — cortex, 3 - medulla. Microscopic section: 1 - cortex, 2 - zona glomerulosa, 3 - zona fasciculata, 4 - zona reticularis, 5 - medulla

2). **Zona fasciculata** is the thickest zone. It consists of narrow cords of polyhedral cells (one or two cells thick). The cytoplasm of the cells is rich in smooth endoplasmic reticulum and lipid droplets. Zona fasciculate produces **glucocorticoids,** mainly cortisol and corticosteron. **These hormones regulate the carbohydrate, protein and lipid metabolism, and also suppress the immune response** by decreasing of number of circulating lymphocytes. Secretion of glucocorticoids is under control of ACTH of adenohypophysis.

3).**Zona reticularis** consists of cells disposed in irregular cords that form an anastomosing network. These cells are smaller than those of the other two layers. Lipofuscin pigment granules in the cells are large and numerous. Zona reticularis is responsible for secretion of small quantities of **androgens and glucocorticoids**. Zona reticularis is under control of ACTH of adenohypophysis.

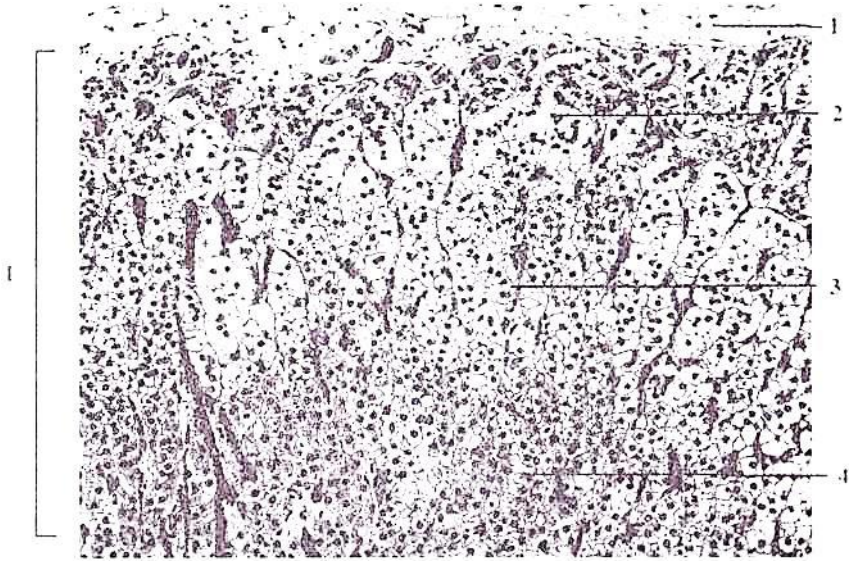


Figure 167. Photomicrograph of adrenal gland. I - cortex, 1 — capsule, 2 - zona glomerulosa, 3 - zona fasciculata, 4 - zona reticularis.

Adrenal medulla.The adrenal medulla is composed of polyhedral chromaffin cells arranged in cords or clumps and supported by reticular fiber network. The adrenal medulla consists **of two types of cells**:

- **epinephrin-secreting cells**, which have smaller, less-electron-dense granules;
- **norepinephrin-secreting** cells, which have larger, more electron- dense granules. Acute physical and psychological stresses initiate release of adrenal medullary hormones (**catecholamines adrenaline, or epinephrine and noradrenaline or norepinephrine**); they act on adrenergic receptors throughout the body particularly in the heart and blood vessels, bronchioles, visceral and skeletal muscle.

Major effects of nonepinephrine and epinephrine: increase heart rate, increase blood pressure, reduce blood flow to viscera and skin, stimulate conversion of glycogen to glucose, increase sweating, induce dilation of bronchioles, increase rate of respiration, decrease digestion, decrease urine production. The adrenal medulla is also responsible for the secretion of enkephalins, opioid peptides, which may be involved in control of pain.

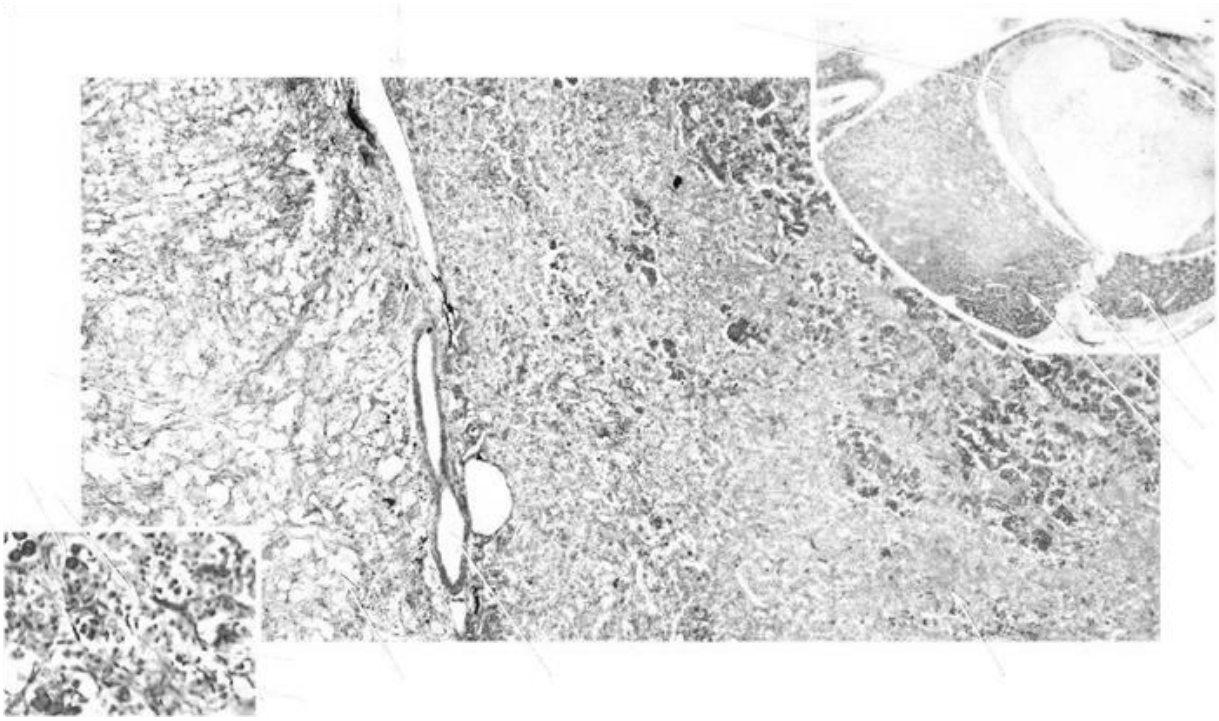
Histogenesis of the adrenal glands.The adrenal glands are derived from 2 embryonic sources:

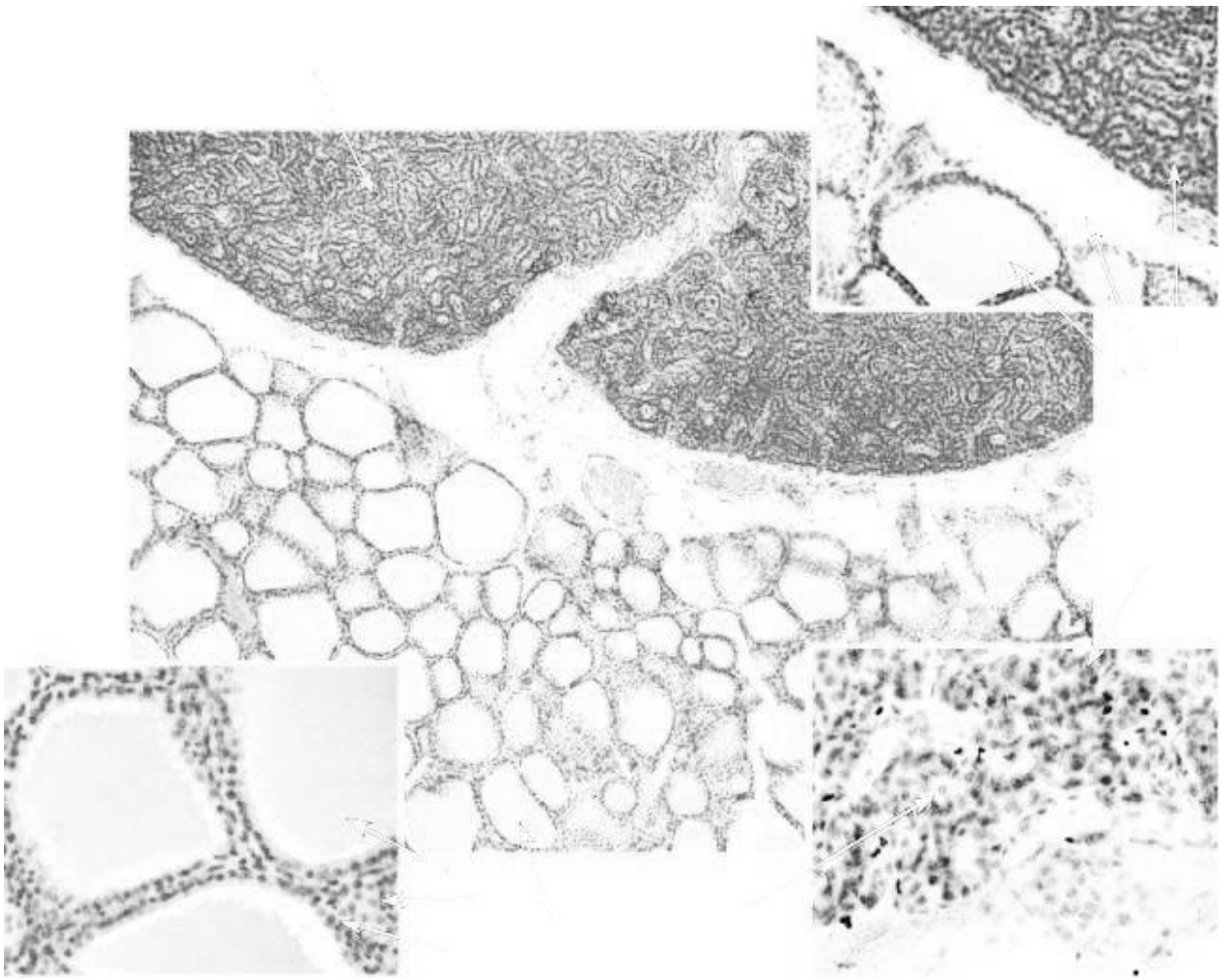
- adrenal cortex is mesodermal, derived from coelomic epithelium;
- adrenal medulla is ectodermal, derived from neural crests.

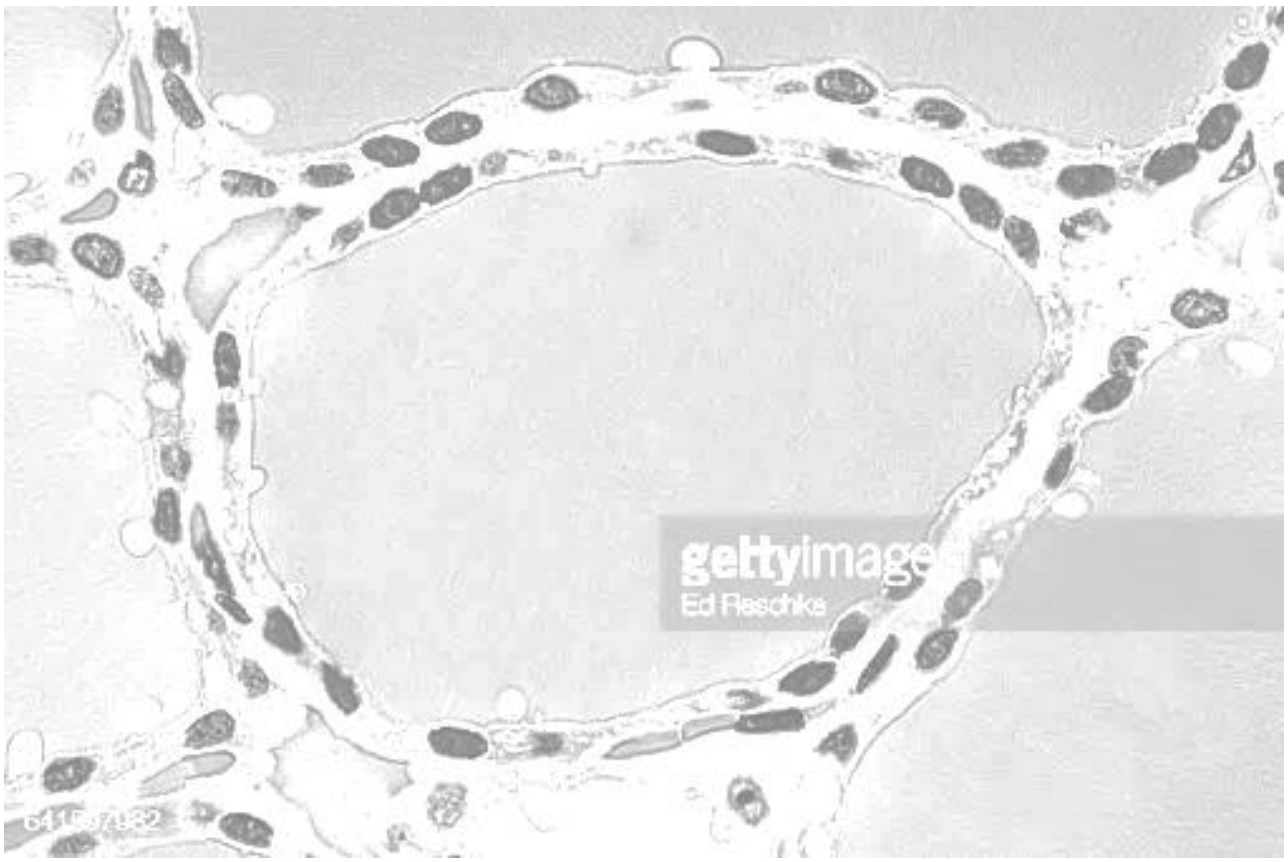
Practical lessons

1.Classification of the endocrine glands. Pineal gland: structure and functions.
2. Hypothalamus nuclei, their endocrine functions, interconnections with hypophysis.
3. Hypophysis: adeno- and neurohypophysis, hormones and their influence on the human body.
4.Pineal gland
5. Thyroid gland: structure and functions.
6. Parathyroid glands: structure and functions.
7. Adrenal glands: structure and functions of the cortex and medulla.

Paint and mark basic histological structure



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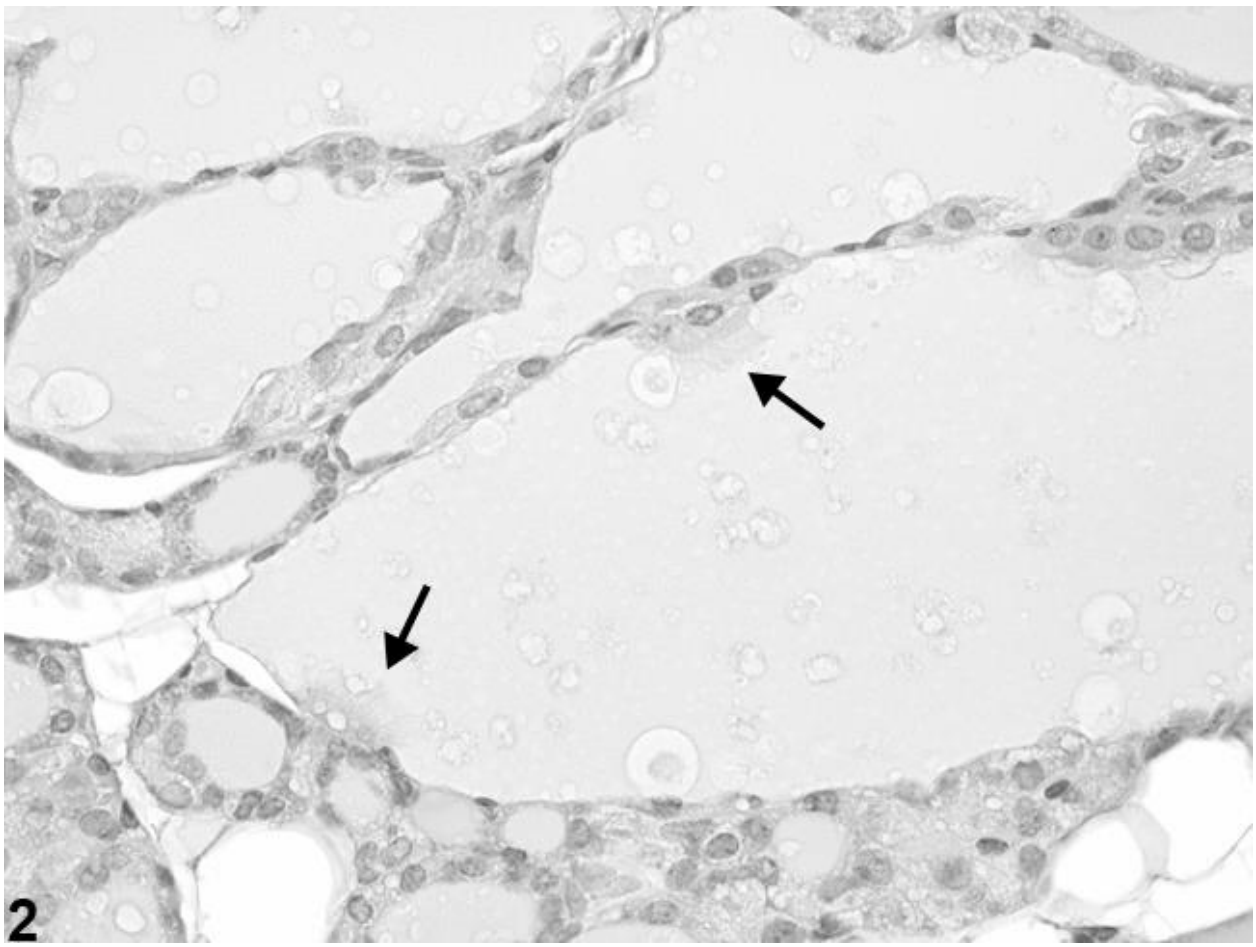
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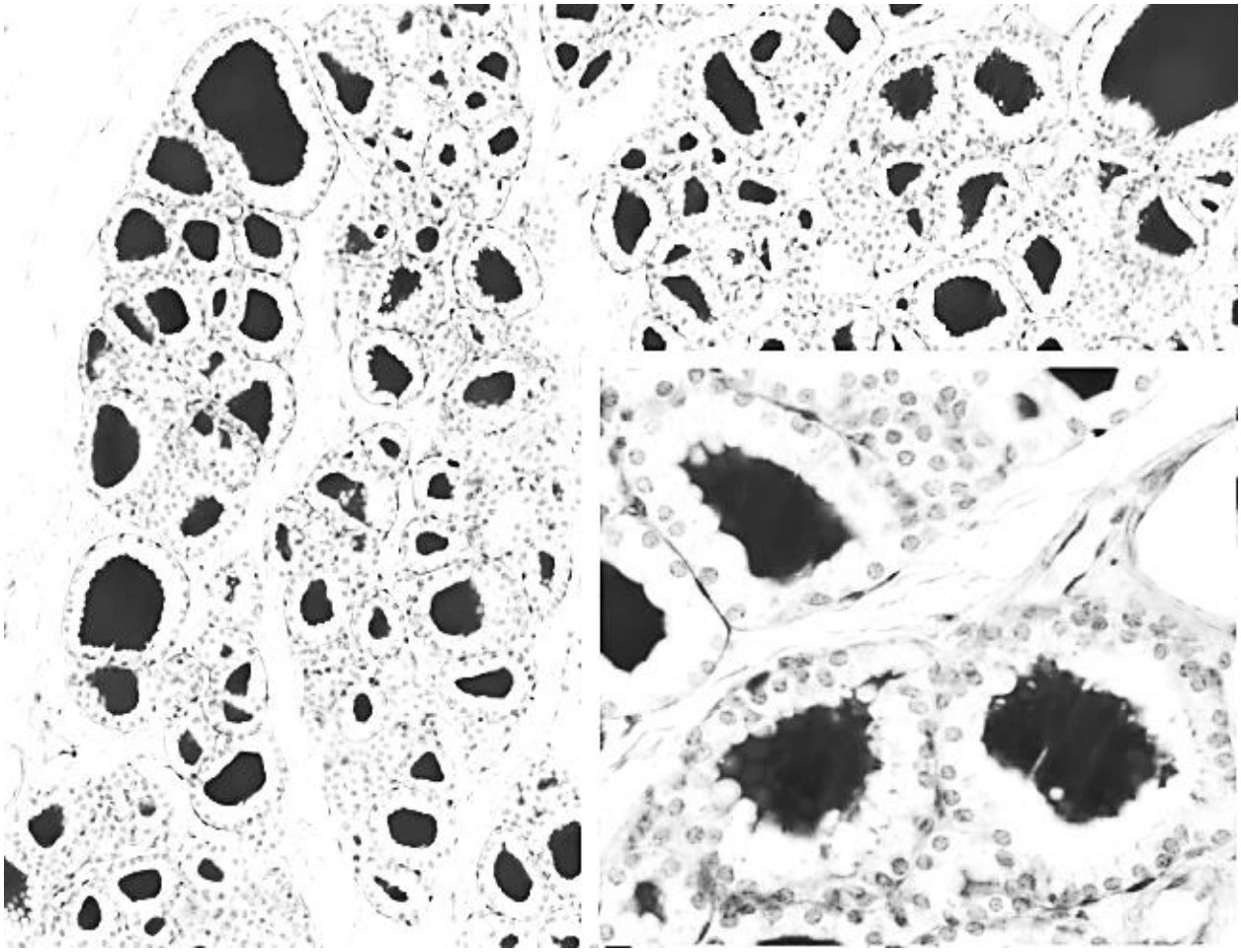

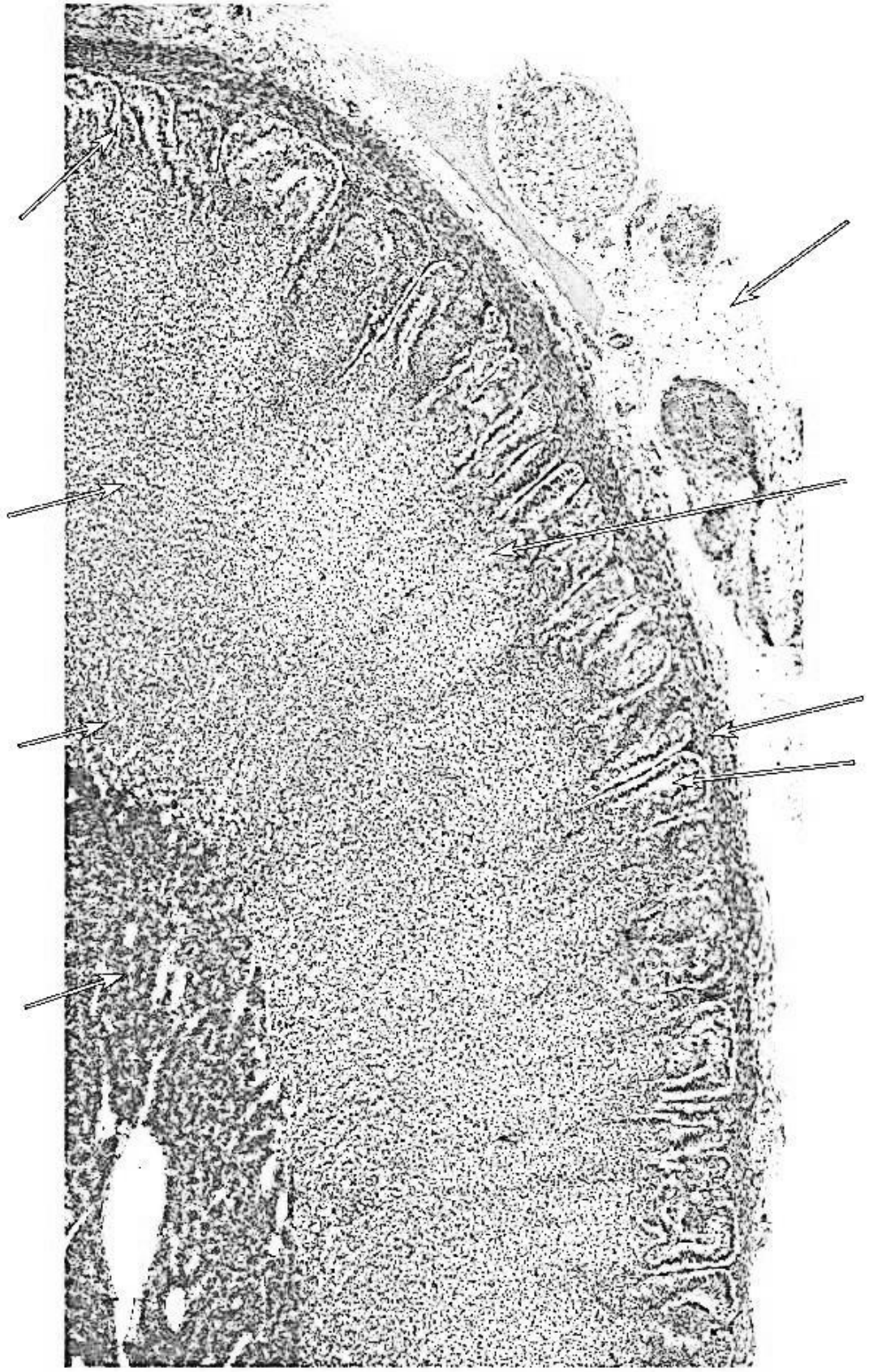

Signature of teacher_____

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